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Small Peptide-Induced Changes in Plasma Membrane and Intercellular Communication

917C0578A Moscow BIOFIZIKA in Russian Vol 36 No 2, Mar-Apr 91 (manuscript received 29 Mar 90) pp 308-312

[Article by S. V. Konev, T. G. Yanchevskaya and N. V. Gamezo, Institute of Photobiology, Belorussian SSR Academy of Sciences, Minsk]

[Abstract] Mechanisms underlying small peptide-enhanced intercellular communication were analyzed in microelectrode and microcytofluorimetric studies on target cells exposed to low peptide concentrations (10E-12 to 10E-6 M). The studies involved drosophila salivary gland cells, L-vasopressin and substance P fragments (Leu-Met = 298 MW; Gly-Leu-Met = 355.2 MW; Phe-Phe-Gly-Leu-Met = 648.5 MW), and related electrotonic potentials to intercellular migration of inorganic ions and fluorimetric monitoring of fluorescein transit between cells. The results demonstrated that each peptide, known to bind to receptors at sites remote from gap junctions, enhanced intercellular exchange of inorganic ions and organic molecules. Enhancement was abolished by treatment of the target cells with 1-ethyl-3(3-dimethylaminopropyl)-carbodiimide, a protein cross-linking agent. These observations were interpreted to indicate that the peptides, acting at sites remote to the gap junctions, induced structural rearrangement in plasma membrane proteins which facilitated intercellular transport, a phenomenon unrelated to membrane potential. Cross-linking immobilzed the membrane proteins and thereby precluded peptide action. Figures 4; references 7: 3 Russian, 4 Western.

Imitation Model of Autoassociative Memory Based on Low-Activity Neural Network

917C0578B Moscow BIOFIZIKA in Russian Vol 36 No 2, Mar-Apr 91 (manuscript received 27 Feb 90) pp 339-343

[Article by A. A. Frolov, A. M. Mushinskiy and M. V. Tsodyks, Institute of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences, Moscow]

[Abstract] Mathematical rationale is presented for imitational modeling of autoassociative memory based on pattern classification of neural networks. The analysis was based on the asumption that statistical sets store information and represent a matrix of graduated synaptic connections underlying autoassociative memories. A pattern map is converted to real-value feature vectors. With optimal network parameters the efficiency coefficient may approach 0.72 and the imitation model gives good agreement with the replica model. Figures 5; references 7: 1 Russian, 6 Western.

Absorption of Millimeter Microwaves by Bacterial Photosynthetic Reaction Centers

917C0598A Moscow BIOFIZIKA in Russian Vol 36 No 1, Jan-Feb 91 (manuscript received 16 May 90) pp 55-59

[Article by B. G. Yemets, P. P. Noks, G. Sh. Margishvili, Ye. V. Belyakov and A. A. Kononenko, Biological Faculty, Moscow State University; Kharkov State University]

[Abstract] An analysis was performed on the absorption of ca. 6.5 millimeter (46 GHz) microwaves by Rhodobacter sphaeroides and Chromatium minutissimum photosynthetic reaction centers in order to assess their relative degrees of hydration. The underlying rationale was the fact that bound and free water differ in absorption of millimeter waves, with bound water failing to absorb ca. 6.5 mm (46 GHz) wavelength. Photosynthetic reaction centers were studied in the presence of detergents and cryoprotectors (glycerol, proylene glycol, DMSO). Determinations of the degrees of hydration showed that Rh. sphaeroides reaction centers exhibited minimal hydration, while Ch. minutissimum reaction centers bound an anomalously high concentration of water. Control studies demonstrated that the differences were not due to the detergent employed. Presumably the results reflected the fact that Rh. sphaeroides reaction centers contain a high content of strongly hydrophobic components, while Ch. minutissimum centers contain the hydrophilic multihemic cytochrome c. These findings confirmed previous studies utilizing SHF dielectrometry. Tables 2; references 17: 15 Russian, 2 Western.

Photoelectrochemical Properties of Platinum Electrodes Bearing Rhodobacter Sphaeroides R-26 Reaction Centers

917C0598B Moscow BIOFIZIKA in Russian Vol 36 No 1, Jan-Feb 91 (manuscript received 15 Apr 90) pp 60-64

[Article by A. A. Solovyev. Ye. Yu. Kats, V. A. Shuvalov, Yu. Ye. Yerokhin and A. N. Kuzmin, Institute of Pedology and Photosynthesis, USSR Academy of Sciences, Pushchino, Moscow Oblast]

UDC 577.37

[Abstract] An assessment was conducted on the photoelectrochemical behavior of platinum electrodes bearing immobilized reaction centers derived from Rhodobacter sphaeroides R-26. The results showed that photocurrents generated by electrodes modified by cysteamine and 2,3-dichloro-1,4-naphthoquine as substrate for the reaction centers were 4- to 5-fold greater than results with electrodes that had only been modified with cysteamine. Incubation of the electrodes with TL buffer (0.01 M tris-HCL, pH 8.0, 0.1 percent lauryldimethylamino-N-oxide) containing reduced cytopchrome c and ubiquinone-10 (UQ-2) enhanced the activity of the electrodes and led to appearance of a rapid component. Periodic rinsing of the electrodes with TL buffer maintained high levels of activity and extended the working life to ca. one month. These observations were interpeted to indicate that the reaction centers retained near-native state and that immobilization did not affect Q_A and Q_B binding sites. Accordingly, these findings indicate that other primary and secondary quinones should be tested to further optimize such electrodes. Figures 3; references 8: 2 Russian, 6 Western.

Interaction of Bacteriochlorophyll and Quinone Electron Acceptors in Rhodobacter Sphaeroides Reaction Centers: Impact of Heavy Water and Aprotonic Solvents

917C0598C Moscow BIOFIZIKA in Russian Vol 36 No 1, Jan-Feb 91 (manuscript received 7 Jun 90) pp 74-77

[Article by Ye. P. Lukashev, G. Sh. Margishvili, A. A. Kononenko and N. I. Zakharova, Biological Faculty, Moscow State University]

[Abstract] An assessment was conducted on the impact of D_2O and aprotic solvents on photoinduced reduction of bacteriopchlorophyll P^+ by Q_A^- and Q_B^- in reaction centers derived from wild type Rhodobacter sphaeroides. Both isotope exchange and addition of aprotic solvent reduced the efficiency of direct e^- transfer from Q_A^- to Q_B, as indicated by diminution in the slow component (τ = 1.1-1.3 sec) of P^+ reduction. In the case of D_2O the effect was attributed to alterations in the hydrogen bond systems of the proteins leading to greater internal rigidity and inhibition of $Q_A^-Q_B$ $Q_AQ_B^-$ transitions. Aprotic solvent exercised a similar effect, attributed to interference with protonation of ionogenic amino acid residues which are responsible for stability of the $P^+Q_AQ_B^-$ complex. The effects of the aprotic solvents corresponded in direct proportion to their hydrophobicity (1.35 to 1.54 in octanol:water system) and inversely to their dipole moments (3.96 to 0.66), resulting in the following ranking: acetonitrile < diethyl ether < pyridine < triethylamine. Figures 1; references 15: 6 Russian, 9 Western.

In Vitro Impact of Low Adaptogen Concentrations on Mouse Bone Marrow

917C0598D Moscow BIOFIZIKA in Russian Vol 36 No 1, Jan-Feb 91 (manuscript received 10 Nov 89) pp 105-108

[Article by S. N. Udintsev, V. P. Shakhov, I. G. Borovskoy and S. G. Ibragimova, Scientific Research Institutes of Pharmacology, Tomsk Scientific Center, USSR Academy of Medical Sciences, and of Applied Mathematics and Mechanics, Tomsk State Unviersity]

[Abstract] An analysis was performed of the physiological effects of low concentration of aqueous preparations of adaptogens, represented by a synthetic analog (SA) of a phenolic compound extracted from Rhodiola rosea and dibazol [sic], on bone marrow etrythoid cells of (CBA x C57BL/6)F_1 mice. Incubation studies demonstrated that clone formation was dependent on adaptogen concentration. At a concentration of 10E-6 M colony formation was inhibited by SA, while at higher dilutions was stimulated. Dibazol showed a similar pattern. Activities were lost after dilutions reduced the concentration of SA to 10E-26 M and dibazol to 10E-31 M. Since stimulation was evident when one molecule of SA or dibazol was available per cell, the data were interpreted to indicate that the effect was secondary and due to changes in solvent (water) structure which were complementary to the molecules in question. These structural changes in the solvent were retained as molecular memory and subsequently translated into action on target cells. Figures 1; tables 1; references 12: Russian.

Sixteenth Higher Educational Institution Student Science Conference "Soil Science and Agricultural Chemistry in Solving Ecological Problems"

917C0506A Leningrad VESTNIK LENINGRADSKOGO UNIVERSITETA: BIOLOGIYA in Russian No 24, Nov 90 pp 93-108

[Selected synopses from the 16th Higher Educational Institution Student Science Conference "Soil Science and Agricultural Chemistry in Solving Ecological Problems", held 12-14 April 1990 at the Soil Department, Biology-Soil Faculty, Leningrad University]

[Excerpts]

Synopses

O. M. Tereshenkov, Ye. V. Babenko, and A. I. Andriyenko

Monitoring Petroleum-Polluted Ecosystems

Leningrad University

The construction and operation of oil fields have an extremely significant effect on the environment in petroleum producing rayons. On the one hand, there are mechanical disturbances to the soil canopy, while on the other there is environmental pollution with petroleum and its byproducts. Methods for recultivating oil-polluted earth that are being used currently do not always aid the development of the processes for their regeneration, and frequently also cause some harm (for example, earth moving of contaminated sections or burning of petroleum at accidental spills). We selected soil samples that were recultivated by various methods (peat enrichment of the soil, earth moving, and cultivation) for our research. The following may be concluded based on the analytical processing, investigation of the spectrophotometric properties, and assessment of the soil's microbiological activity, as well as comparison of data with the content of residual petroleum. The rate of biodegradation of petroleum is slowed almost 2-fold in cases of recultivation of petroleum-polluted soil by means of earth moving (filling with sand) in the central taiga of Western Siberia. The spectrophotometric characteristics of air dried soil samples make it possible to determine the depth of petroleum penetration by means of soil profiling. The spectral curves of petroleum polluted samples differ dramatically from their non-polluted counterparts in their external appearance, and the significance of spectral brightness coefficients diminishes. The areals of petroleum polluted soils can be clearly seen from aerial photographs (fresh spills from the direct signs, primarily the tone and form; old spills more frequently from indirect signs). Mechanized processing of the aerial photographs makes it possible to decipher areals of petroleum polluted ecosystems with a great degree of reliability by using the statistical characteristics of the contours isolated and tp determine the areas of accidental spills.

Ye. N. Vinogradova, Ye. A. Mukha, E. I. Gagarina, R. I. Bayeva, and A. D. Gorbovskaya

Effect of "Fosforit" Production Association on Surrounding Territory

Leningrad University

The rayon in question is northwest of the Russian platform and occupies the watershed between the Luga and Narva rivers. The plant consists of mining and refining enterprises. The phosphorites are obtained by open mining methods; reforestation is being conducted in order to restore the disturbed territories. The ground of the banks has a wide variety of properties, and as a whole it is suitable for biological recultivation. The original enzymatic activity of the soils is very low and is manifested only in the activity of dehydrogenase and invertase. Peat enrichment of the banks is being conducted in places in order to increase the enzymatic activity. The young areas are being heavily cultivated, with up to 10 mm of annual growth in the humus horizon. The humus content has reached 2 percent within the last six years; the humus type is humate-fulvate. The biological activity of the cultivation was assessed by the intensity of the nitrogen mineralization processes, the cellulose decomposition rates, "respiration" of the ground, and the number of bacteria and fungi. It was found that the biological activity changes throughout the vegetation period, that it depends on the physical and chemical properties of the ground, and that it increases with the age of the banks.

The "Fosforit" Production Association not only destroys the soil canopy, but it also pollutes the nearby undisturbed soils, especially those in direct proximity to the plant to the north and northwest. The effect of the plant can be felt up to 15 km away. It is reflected in the change in the species composition of the plants and in the covering of the soils with wastes carried from the open surfaces of the banks and during excavation work. In addition, there is alkalization of the soils and a noticeable rise in phosphorus, which is accompanied by an increase in the biological activity, cellulose decomposition rate, and nitrate accumulation. Acidification of the soils has been noted near the refinery plant due to acidic byproducts. This diminishes the microbiological activity and intensity of nitrogen mineralization. Soil pollution also alters the soil properties, which is expressed in their physical and chemical indicators, and it alters the composition of organic matter by increasing the content of the humic acids that are bound with calcium.

Comparative Characteristics of Influenza Epidemics

917C0554A Alma-Ata ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian No 2, Feb 91 pp 10-11

[Article by V. K. Urazov, Scientific Research Institute of Epidemiology, Microbiology and Infectious Diseases, Alma-Ata]

UDC 616.921.5-036.22(574.31)

[Text] Before going on to a detailed examination of the basic characteristics of the epidemic process in the Karaganda integrated iron-and-steel works, we will define its place in the structure of all influenza and ear, nose and throat morbidity in the adult population of Temirtau. Analysis shows that the workers of the iron-and-steel works, who make up less than a fifth of the city's adult population, are responsible for 30 to 46 percent of these illnesses.

In the period from 1979 to 1985 four epidemics of type A influenza were recorded in the city and at the steel works (1979-1980, 1981-1982, 1983 and 1985). Their duration averaged five weeks. In this case this indicator was more stable at the steel works than in the city, where it varied from four to nine weeks. Morbidity usually peaked in the third to fourth week. The year 1983 was an exception, when it peaked in the city in the last week from the beginning of the outbreak, and in the steel works it did so in the first week. Moreover morbidity varied within wide limits during those periods: from 0.4 to 6.8 percent in the adult population of the city, and from 2.8 to 12.9 percent among workers of the steel works (see table).

Influenza and Ear, Nose and Throat Morbidity of the Population of Temirtau and Workers of the Karaganda Integrated Iron-and-Steel Works in 1979-1985

Epidemic Season, Epidemic Etiology	Morbidity (%)			Proportion of Influenza in Annual Morbidity
	Annual	Epidemic	Nonepidemic	
1979-1980	13.4/25.4	6.8/12.8	6.6/12.6	50.7/50.8
A (H3N2)				
1980-1981	10.6/23.7	3.4/ 6.0	7.2/17.7	32.1/25.4
B				
1981-1982	7.9/23.1	1.1/ 2.5	6.8/20.6	13.3/10.8
A (H1N1)				
1982-1983	9.5/25.5	0.4/ 2.8	9.1/22.8	5.0/10.0
A (H3N2)				
1983-1984	12.6/31.9	4.1/10.7	8.5/20.3	31.8/33.4
B				
1984-1985	8.8/24.6	2.5/4.5	6.3/20.1	28.4/21.0
A (H3N2)				
Averages, with confidence limits	10.4/25.7	3.0/6.5	7.4/19.0	26.9/21.0
	(8.2 + 12.6)/(22.1 + 29.3)	(0.4 + 5.6)/(3.8 + 9.2)	(6.3 + 8.5)/(15.7 + 22.3)	(12.5 + 45.4)/(15.6 + 27.6)

Such a dramatic difference in indicators is explained by different intensities of the epidemics over the observed time interval. For example influenza morbidity was recorded at the highest level in 1979-1980: 6.8 percent in the adult population of the city, and 12.9 percent among steelworkers. In subsequent years morbidity declined, and in 1983 it was recorded within 0.4 and 2.8 percent.

The same features are also noted in an analysis of type B influenza morbidity: 3.4 and 4.1 percent in the adult population in 1981 and 1984, and almost twice higher (6.0 and 10.7 percent) among employees of the steel works.

Epidemics of this type lasted an average of eight weeks in the city and seven weeks at the steel works. Moreover the duration of type B influenza was two to three weeks longer than type A influenza.

The facts presented in the table reflect an etiological approach to analyzing the entire group of acute respiratory viral infections, which made it possible to obtain two groups of indicators—true or epidemic influenza morbidity, and nonepidemic morbidity involving other ear, nose and throat diseases with etiology other than that of influenza. During the period in question, epidemic influenza morbidity in the adult population of the city averaged 3.0 percent, while among steelworkers it was 6.5 percent, or 2.16 times higher. Incidentally, the average multiannual indicator of nonepidemic morbidity was also 2.5 times higher among steelworkers (19.0 percent) than in the adult population of the city (7.4 percent).

The dynamics of the proportion of influenza in annual influenza and ear, nose and throat morbidity in 1979-1985 generally reflect the intensity of the epidemic process associated with influenza in the city and at the steel works.

For example the largest epidemic was recorded and the highest proportion of influenza was noted in 1979-1980 (50.7 and 50.8 percent). A decrease in the intensity of the influenza epidemic is observed in subsequent years, accompanied by a decrease in the proportion of influenza in annual morbidity consisting of acute respiratory infections. In 1983 these values did not exceed 5.0 and 10.0 percent for the city and steel works respectively, while their average over the period in question was 21.6 and 26.9 percent. We can see that the remaining three-fourths of the morbidity consists of nonepidemic acute respiratory infections of etiology other than that of influenza.

In order to refine the influenza and ear, nose and throat morbidity trends, we inspected monthly morbidity records for 1969 through 1985, subjected to regression analysis [1]. The period in question contained 12 type A influenza epidemics and six type B influenza epidemics.

It was established that epidemic morbidity of type A influenza tended to decrease in both observation groups, the decrease being most clearly pronounced among steelworkers. On the other hand epidemiological morbidity associated with type B influenza increased. The results of the analysis also suggest pronounced growth of nonepidemic morbidity. Moreover in both cases the epidemic process was especially evident among steelworkers.

The differences mentioned above are tightly correlated with the state of collective immunity [2]. Thus, immunity to type A influenza is noted to be high in all areas in recent years, which has naturally promoted a decrease in its occurrence.

References

1. Vasilyev, K. G., Reynaru, I. K. and Yagodinskiy, V. N., "Analiticheskaya epidemiologiya" [Analytical Epidemiology], Tallinn, Valgus, 1977, pp 282.

2. Ismagulov, A. T., "Tendency for Development of the Epidemic Process Associated With Influenza," in "Epidemiologicheskiy nadzor za grippom i prognozirovaniye epidemiy" [Epidemiological Surveillance of Influenza and Prediction of Epidemics], Leningrad, pp 107-110.

Organization of Specific Clinical, Epidemiological and Laboratory Examinations for Leptospirosis

917C0554B Alma-Ata ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian No 2, Feb 91 pp 13-15

[Article by K. V. Shevchenko, B. V. Makhnin, G. I. Larionov, A. S. Grube and V. B. Zaykovskiy, Central Asian Scientific Research Institute of Plague Control, Alma-Ata]

UDC 616.986.7-036.21

[Text] Most places serviced by the Alma-Ata Railroad are within the administrative borders of oblasts in the south and southeast of the republic, where many authors have noted presence of active natural and anthropogenic leptospirosis foci in different years. Their present activity is indirectly confirmed by data from epidemiological and veterinary services on morbidity among people and agricultural animals.

Considering the epidemic and epizootic situation, and the status of laboratory diagnosis and of the fight against leptospirosis in these oblasts, as of 1985 the Alma-Ata Plague Control Station assumed the function of providing consultative and practical assistance to public health institutions of the Alma-Ata Railroad in organizing measures to reveal and prevent leptospirosis among railroaders and their families. It is difficult to find detailed recommendations in available literature and in directive and methodological documents on how such work should be carried out by rail transportation's medical service; this is excluding the sporadic railway ministry instructions that have little to do with these problems.

We proposed and tested a version of a model of clinical epidemiological and laboratory diagnosis of leptospirosis in medical institutions of the Alma-Ata Railroad taking account of the unique features of a railroad department. We based the selection of our approaches on a currently effective order of the USSR Ministry of Health (No 1152 dated 13 November 1979), and on its recommendations and those of the Ministry of Railways on other especially dangerous infections. Our establishment of a centralized leptospirosis laboratory under the Alma-Ata Plague Control Station was an important part of this model's implementation. Permission to establish this laboratory, which contains facilities for serological analysis of materials from people and rodents, was granted by the Central Procedural Commission of the USSR Ministry of Health. A mobile laboratory capable of primary processing of specimens was used in exploratory research conducted in anthropogenic foci. Microagglutination and lysis reactions were carried out with diagnostic sets of 13 *Leptospira* strains obtained from the Experimental Medicine Institute imeni N. F. Gamaleya of the USSR Academy of Medical Sciences.

We wrote and sent a letter of instruction to the railroad's medical institutions on organizing specific laboratory analysis for leptospirosis with the purpose of providing assistance in specific testing for this infection among patients hospitalized in infection, therapeutic, surgical and other departments and possessing diagnoses warranting such testing: suspected leptospirosis, typhoid fever, ear, nose and throat diseases, meningitis, viral hepatitis, rickettsiosis, acute kidney disease, brucellosis, acute conjunctivitis and some others, if a suspicion of leptospirosis arose while in hospital. Procedures for sampling and transporting various materials to the centralized leptospirosis laboratory, and samples of referral cards, notices and zootic infection focus epidemiological examination cards were attached to the letter.

In accordance with these instructions, when a patient suspected of leptospirosis is detected, collection of material for laboratory analysis is mandatory; such material must be sent by available means of transportation to the central leptospirosis laboratory for determination of *Leptospira* antibodies. In the event of a positive result a

notice is transmitted to the railroad epidemiological station, which is the coordinating center for many infections, and to the therapeutic-preventive institution in which the patient or suspected carrier was discovered. On receiving the results of the laboratory analysis, and after comparing it with clinical analyses and objective examination data, this institution then confirms or rejects the previous diagnosis, and implements further measures to treat the patient. Paired sera are also mandatorily sent out for analysis.

In order to study a leptospirosis focus and carry out a package of veterinary and other measures within it, the epidemiological department of the railroad epidemiological station implements the corresponding measures both through its own efforts and through those of local epidemiological and therapeutic-preventive institutions. Each case of illness confirmed by laboratory analysis is subjected to epidemiological examination; epidemiological cards are mandatorily filled out, and copies are sent to the railroad epidemiological station. In addition to this, division and line epidemiological stations determine the epizootic situation among agricultural animals in the given population center, rayon and section, and the incidence of leptospirosis among people. Materials from territorial public health and veterinary service agencies are used additionally. Specialists from the Central Asian Plague Control Institute are brought in for consultation as necessary.

As a result of the specific clinical and epidemiological leptospirosis examinations we organized in medical institutions of the Alma-Ata Railroad, this infection was discovered among a number of patients with other diagnoses. For example one patient with a diagnosis of brucellosis had a positive microagglutination and lysis reaction with a 1:100 dilution of *Grippotyphosa* serological group. Paired sera sampled after several days revealed growth of antibody titers. In another case a patient with a diagnosis of "viral hepatitis" had a positive result with a 1:400 titer of *Pyrogenes* serological group, with further growth observed subsequently in paired sera.

Blood sera from workers at departmental subsidiary farms—a total of 163 persons—were analyzed for the purposes of retrospective analysis of the incidence of leptospirosis in different groups of railroaders. Positive results were obtained in 6.1 percent of the sera, which contained antibodies identified as being in the following serological groups: *Grippotyphosa*—3.6 percent, *Icterohaemorrhagiae*—1.2 percent, *Cynopteri*—0.6 percent, *Pyrogenes*—0.6 percent.

Eight hundred seventeen rodents of different species were studied in an effort to find natural and anthropogenic leptospirosis foci. The greatest incidence of the disease was found among gray rats, 25 percent of which possessed *Icterohaemorrhagiae*, *Grippotyphosa* and *Pomona* serological group antibodies at titers of 1:100-1:800. Five physicians and eight laboratory technicians of the newly organized laboratory were trained in the methods of laboratory diagnosis in addition to diagnostic analyses. A number of seminars were also conducted, and lectures were given locally to specialists of the railroad's therapeutic institutions.

Our model of specific clinical, epidemiological and laboratory leptospirosis examination does not conflict with the basic principles of epidemiological surveillance for this infection. Attraction of the attention of the railroad's medical service to the problem of leptospirosis as one component of infectious morbidity and practical introduction of laboratory diagnostic methods may be said to be important results in the first stage of this effort. In testing the model, we revealed the following: poor participation of some medical institutions in this work, and reduction of the value of laboratory results and their retrospective nature due to the great distance this information had to travel from a number of population centers.

As we learn more about the role of leptospirosis in infectious morbidity, we feel that it will be necessary to improve our model by expanding the network of laboratories working out of departmental epidemiological stations and by strengthening interaction with medical institutions of both the union and republic health ministries.

Interpretation of the Etiology of Influenza Outbreaks in Semipalatinsk Between 1985 and 1987

917C0554D Alma-Ata ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian No 2, Feb 91 pp 23-24

[Article by O. P. Kizub, G. Ye. Khripunova, T. D. Ukbayeva, A. T. Ismagulov and A. P. Myatchina, Scientific Research Institute of Epidemiology, Microbiology and Infectious Diseases, Alma-Ata]

UDC 616.921.5(574.41)

[Text] We studied the proportionate incidence of influenza in epidemic and interepidemic periods among residents of Semipalatinsk between 1985 and 1987.

We analyzed 1,263 nasopharyngeal washings and 1,829 paired blood sera from patients suffering influenza, ear, nose and throat diseases and pneumonia. The virological method, the fluorescing antibodies method and the hemagglutination inhibition test were used for influenza diagnosis.

Chick embryos were used for virological study of material obtained from ear, nose and throat patients.

A total of 193 persons were subjected to virological analysis in the first quarter of 1985. Eleven hemagglutinating agents were isolated. Following identification with standard sera in the hemagglutination inhibition test, they were classified as type A (H3N2) influenza virus. In serological tests of 296 paired sera from the blood of patients, a 4-fold (and higher) increase in the titer of antibodies to type A (H3N2) influenza virus antigen was established among 20.6 +/- 2.3 percent of the subjects, while an increase in the titer of antibodies to type A

(H1N1) and type B virus was observed among 3.4 +/- 0.9 percent and 1.4 +/- 0.6 percent of the patients respectively.

Sixty-seven paired blood sera from ear, nose and throat patients were studied in the interepidemic period (from April to September 1985). Four-fold (and higher) growth of the titer of antibodies to type A and B influenza virus was established among 68.9 +/- 3.4 percent of the subjects. A rise in incidence of influenza and of ear, nose and throat diseases was observed beginning in October. In the fourth quarter of 1985, 127 paired sera were subjected to the hemagglutination inhibition test. Type A (H1N1) influenza was diagnosed in 7.2 +/- 2.2 percent of patients under observation, type A (H3N2) was diagnosed in 5.5 +/- 1.0 percent, and type B was diagnosed in 3.9 +/- 1.7 percent.

Two hundred forty-six paired sera were studied in the first quarter of 1986. Influenza infection was diagnosed in 60 (24.4 +/- 2.6 percent) patients. Ninety-six paired sera were analyzed in the interepidemic period (from April to September 1986). A diagnostically significant increase in the titer of antibodies to type A and B influenza virus was not noted.

In Semipalatinsk, the increase in incidence of influenza and ear, nose and throat diseases was observed in November 1986. Morbidity peaked in December. Four hundred and twenty cases of ear, nose and throat disease and 97 cases of influenza were recorded in this month (per 10,000 residents). Patients consisted primarily of children up to three years old. The first strain of type A (H1N1) influenza was isolated from child O. who was one year and two months old. His disease course was acute, and his temperature climbed to 38.8°C. A cough appeared immediately, pharyngitis was evident, and regional lymph nodes were enlarged. The child was admitted to the clinic on the fourth day of illness. The hemagglutinating agent was identified by titration with standard immune sera as influenza virus with the antigenic formula A (H1N1). The etiological role of the isolated virus was confirmed by positive serum conversion.

A young girl A., eight years old, was admitted to the clinic on the day after falling ill. Her disease course was acute, and she suffered high temperature, headaches and catarrhal phenomena. On that same day a nasopharyngeal washing was taken for the purposes of chick embryo infection. The hemagglutinating agent was isolated in the very first passage. Its titer was 1:16. The strain was classified as type A (H1N1) influenza virus, and positive serum conversion was established in blood serum.

Virological examination of 85 samples taken from patients revealed 17 hemagglutinating agents, which was 20.0 +/- 4.4 percent. When titration was performed in the hemagglutination inhibition test with standard immune sera, they were identified as influenza virus with the antigenic formula A (H1N1). In the last two months of 1986 139 paired blood sera were subjected to the hemagglutination inhibition test. Positive serum conversion in relation to influenza virus was established for 33 (38.1 +/- 4.0 percent) patients. Of this number, 50.9 percent were serum conversion to virus A (H1N1), 37.7 percent to A (H3N2), and 11.3 percent to B.

Serum conversion to influenza virus was determined in the first quarter of 1987 in 33.02 +/- 4.5 percent of the subjects. This included conversion to serotype A (H1N1) and 24.8 +/- 4.1 percent, to A (H3N2) in 5.5 +/- 2.0 percent, and to B in 2.8 +/- 1.6 percent.

The increase in frequency of serum conversions to type A (H1N1) influenza virus is evidence of its extensive circulation among residents of Semipalatinsk in late 1986 and early 1987.

A diagnostic increase in antibodies to type A (H3N2) influenza virus was revealed in the interepidemic period (April-September 1987) among 11.2 +/- 4.5 percent of the examined children, which was apparently the product of active circulation of this antigenic variant in the child population of Semipalatinsk.

The etiological relationship of the epidemic to influenza virus of this serotype was also confirmed by serological analysis of 43 samples of paired blood sera from influenza and ear, nose and throat patients in the fourth quarter of 1987. Four-fold (and higher) growth of the titer of antibodies to influenza virus was established for 32.6 +/- 7.0 percent of the subjects. Of this number, 57.1 percent were characterized by serum conversion to type A (H3N2) influenza virus.

These data show that type A and B influenza virus is widespread among residents of Semipalatinsk even in periods between epidemics.

Chemiluminescent Analysis of Kinetics of the Generation of Active Forms of Oxygen by Whole Blood Cells in Substituted Exfusions of Blood

917C0491 Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 316 No 1, Nov 90 (manuscript received 29 Jan 90) pp 247-251

[Article by K. I. Pukhov, G. V. Makarskaya, Ye. I. Yakhnina, Ya. I. Pukhova, Institute of Biophysics, Siberian Department, USSR Academy of Sciences, Krasnoyarsk]

UDC 577.13+611.018.5

[Abstract] Features of the kinetic characteristics of the generation of AFO by leukocytic cells in various states of the body, as well as the possibility of using substituted exfusions of blood as a means of restoring the functional activity of leukocytes and reversing immunodeficient states, are said here to have been studied for the first time. AFO generation was measured with luminol-dependent chemiluminescence, which is the most sensitive method of assessing the rate of the leukocyte formation of active forms of oxygen (AFO), because it is based on the recording of the flux of photons formed when luminol is oxidized by AFO. The experimental data that were obtained were statistically processed by computer with the Student's t-test and regression analysis. A typical chemiluminogram for a healthy individual has a single maximum that is achieved within 25-30 minutes. The kinetic characteristics of the chemiluminograms of the 12 gastroduodenal ulcer patients in the study differed from those of the 26 essentially healthy test subjects in that a maximum appeared within 26-30 minutes, and was followed by a second maximum. Consistent differences between the two groups were found in the *S, S/L, S/F, I, I/L,* and *I/F* parameters. Lower specific activity of the total chemiluminescent response and of its intensity per leukocyte and phagocyte in the ulcer patients indicated lower cellular immunity and the development of a secondary immunodeficient state. Analysis of AFO generation in various blood samples demonstrated that the highest values for *I, I/L, I/F, S, S/L* and *S/F* were noted in blood samples during blood loss and did differ from those in whole blood samples taken after reinfusion or in samples from the essentially healthy subjects, with the phagocyte population remaining stable during all stages of plasmapheresis. That indicates that the primary mechanism for the reversal of immunodeficiency as the number of procedures grew was the constant replenishment of the pool of phagocytosing cells as a result of their drainage from the blood-storing organs and the replacement of cellular generations induced by periodic substituted blood loss. Restoration of the chemiluminescent response of the cells bore a positive correlation with the complete healing of the ulcers, which was monitored by fibrogastroduodenoscopy. Figures 4; references 11: 7 Russian, 4 Western.

Laser-Mechanical Suture With a Controllable Compression Time

917C0554E Alma-Ata ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian No 2, Feb 91 p 70

[Article by O. K. Skobelkin, I. V. Korotkiy, V. V. Dorofeyev, B. D. Tleuf and V. V. Korotkiy, Scientific Research Institute of Laser Surgery, USSR Ministry of Health, Moscow]

UDC 616-089:615.849-19

[Text] Significant progress has been achieved in recent years in surgery on the gastrointestinal tract owing to development and introduction of suturing apparatus into clinical practice. An entire series of such apparatus is available today, and it is now firmly within the arsenal of surgeons carrying out operations on the esophagus, stomach and intestine.

Two types of apparatus are basically used in our country and abroad—circular and linear. Despite certain shortcomings inherent to each of these types of suturing apparatus, in comparison with manually applied sutures they create completely different and more favorable biological conditions for regeneration in sutured tissues, which proceeds predominantly in the manner of primary tensioning [1].

According to published data [2,3], hemorrhaging from the line of sutures into the lumen of the organ or into the free peritoneal cavity is the most frequent postoperative complication observed with the use of such an apparatus. Several attempts to eliminate this shortcoming by increasing the frequency and number of rows and changing the arrangement of staples in a suture were unsuccessful, since this unavoidably worsened circulation in the sutured tissues, threatening the integrity of the sutures. This is why finding the most sensible means of connecting together surgical tissues while providing dependable hemostasis and good circulation in the vicinity of the suture is an extremely important problem. These favorable conditions are achieved to the greatest degree by laser-mechanical sutures formed by means of a laser beam combined with a suturing apparatus [4].

We developed a new, original laser suturing apparatus characterized by a perpendicular arrangement of staples in relation to the suture line. The apparatus makes it possible to apply a mechanical suture such that the staples hook onto continuous ligatures extending along both sides of the margins of the sutured tissues. This ensures uniform compression of tissues along the suture line.

The apparatus was tested experimentally on 132 animals (rabbits). A mechanical suture was applied in combination with dissection of the wall of a hollow organ with a traditional scalpel, with a CO_2 laser beam and with an AYG-neodymium contact laser. Nichrome-wire and absorbable catgut thread were used in the apparatus as additional suturing material determining the time of compression.

The quality of the suture applied by means of the apparatus we developed was studied in acute and chronic experiments (on the 7th, 14th, 21st and 30th days after an operation). The research results showed that good hemostasis is achieved in the suture with the use of both absorbable catgut and Nichrome thread combined with traditional and laser dissection of tissues. However, on the 7th and 14th days after the operation, a pronounced infiltrative spindle was noted, together with areas of ulceration of the mucosa, owing to impairment of circulation in tissues near the suture.

Pneumocompression tests on sutures revealed that physical tightness was greatest when the apparatus was used with absorbable thread in combination with dissection of tissues with a CO_2 laser. The average maximum pressure endured by such a suture on the 14th and 21st days after the operation was 110-120 mm Hg, while when Nichrome thread was used, the average maximum pressure was 96-98 mm Hg.

Thus preliminary research on use of the new laser suturing apparatus together with absorbable thread revealed a possibility for controlling the time of compression, which is the basis for good hemostasis and circulation in the vicinity of a combined laser-mechanical suture.

References

1. Gritsman, Yu. Ya., "Mechanical Suture and Gastric Resections," Dissertation in Pursuit of the Academic Degree of Doctor of Medical Sciences, Moscow, 1961.

2. Kulchitskiy, P. Ye., Olekseyenko, V. V. and Shaposhnikov, V. A., ZDRAVOOKHRANENIYE TADZHIKISTANA, No 5, 1968, pp 25-28.

3. Mushegyan, S. A., Melkumov, B. A. and Kulkova, I. A., in "Mater. nauch. konf., posvyashch. probleme anastomozov v zheludochno-kishechnoy khirurgii" [Proceedings of a Scientific Conference Devoted to the Problem of Anastomoses in Gastrointestinal Surgery], Kurgan, 1966, pp 41-43.

4. Skobelkin, O. K., in "Tez. Mezhdunarodnogo simpoziuma po primeneniyu lazerov v khirurgii i meditsine" [Abstracts of an International Symposium on Laser Use in Surgery and Medicine], Moscow, 1988, Part 1, pp 3-5.

Laser Therapy and Death From Ventricular Fibrillation in Coronary Heart Disease

917C0599A Moscow SOVETSKAYA MEDITSINA in Russian No 4, Apr 91 (manuscript received 5 Oct 89) pp 3-5

[Article by N. N. Kipshidze, G. E. Chapidze, L. A. Marsagishvili, M. R. Bokhua and T. G. Akhobadze, Scientific Research Institute of Clinical and Experimental Therapy, Georgian SSR Ministry of Health, Tbilisia]

UDC 616.127-005.8-036.8-06:616.12-008.318-085.849.19-032.14-036.8-07

[Abstract] Various modalities of helium-neon laser blood irradiation were monitored for efficacy in patients with coronary heart disease. The experimental and control

patients were reprsented by a cohort of 300 males and females with a mean age of 57.4 years who had sustained a myocardial infarction. The patients were subdivided further on the basis of the incidence of extrasystoles per day. The results demonstrated that laser therapy (LT) reduced the incidence of extrasystoles to 0.6 percent during the first 24 h versus 6.7 percent in control patients. Mortality during hospitalization in the LT group was 4 percent versus 10 percent in control patients, while the respective two year mortality figures were 10 and 28 percent. These observations demonstrated that blood irradiation with helium-neon laser can be recommended for management of patients with myocardial infarction in an attempt to minimize the incidence of ventricular fibrillation. References 4: 1 Russian, 3 Western.

Cardiovascular Disease Mortality in Rural Region

917C0599B Moscow SOVETSKAYA MEDITSINA in Russian No 4, Apr 91 (manuscript received 2 Mar 90) pp 34-36

[Article by R. I. Shmurun and B. D. Kovalev, Volkhov Centralized Pathoanatomic and Therapeutic Departments, Novoladoga Rayon Hospital, Leningrad Oblast]

UDC 616.1-036.88-02-07(470-22)

[Abstract] An epidemilogic survey of death statistics from cardiovascular pathology at the Novoladoga Hospital, an 80 bed facility, showed 16.9 percent of the deaths were due to myocardial infarction, 1.6 percent to chronic cornary heart disease, 4.62 percent to cerebrovascular diseases, 0 percent to hypertension, and 4.1 percent to rheumatic heart disease. The reason that no deaths were directly attibuted to hypertension was the fact that this pathognomic feature accounted for 52.7 percent of deaths due to myocardial infarction and 75 percent of the deaths from cerebrovascular disease. Comparison with urban statistics showed that these figures were in general lower, except in the case of rheumatic heart disease. The latter was attributed to the fact that managment of the rheumatic process was not as aggressive as in urban settings. References 26: 12 Russian, 14 Western.

Followup of Pancreatic Status in Chernobyl Cleanup Personnel

917C0599C Moscow SOVETSKAYA MEDITSINA in Russian No 4, Apr 91 (manuscript received 17 Apr 90) pp 55-56

[Article by P. N. Lyubchenko, Ye. B. Dubinina, A. L. Roslov, R. S. Tishenina and V. N. Feofanova, Moscow Oblast Clinical Scientific Resarch Institute imeni M. F. Vladimirskiy]

UDC 616.37-008.6-02:614.867(477)

[Abstract] Followup studies on 123 patients (113 men, 10 women), 20 to 45 years old who had participated in the Chernobyl cleanup efforts were performed to assess pancreatic status. The study was felt to be warranted in view of reports that this organ is relatively radioresistant. Exposures ranged from 24.6 to 9.8 rem, although in 10 cases (mostly women) the level of actual exposure could not be ascertained. The combination of clinical chemistries and ultrasonic examination of the pancreas showed evidence of chronic pancreatitis in 20 (16 percent) of the patients. Laboratory findings included elevated blood trypsin levels in 27.1 percent of the patients, elevated urine amylase in 42.5 percent, and morphologic changes in the pancreas of 18.7 percent of the subjects. References 12: 10 Russian, 2 Western.

Problems in Rendering Medical Aid in Disasters

917C0304A Moscow TERAPEVTICHESKIY ARKHIV in Russian Vol 62 No 10, Oct 90 (manuscript received 13 Mar 90) pp 3-5

[Article by V. D. Fedorov, Surgery Institute imeni A. V. Vishnevskiy, USSR Academy of Sciences, Moscow]

UDC 617-001.3-082

[Text] Problems with providing medical aid in various natural, industrial and transportation disasters have started to trouble the public and the state agencies of many of the world's developed countries in recent years. The reason for this lies in growth of the frequency of major accidents in high-output production operations, in rail and air transportation, on gas and oil pipelines and at nuclear power plants, plus the large number of serious natural disasters, with earthquakes primary among them (the earthquakes in the vicinities of Ashkhabad, Tashkent, and Skoplje, in Mexico, in the northern regions of Armenia, and elsewhere).

Special services for quick response to such situations have been created in a number of Western countries (United States, FRG, France and others). They not only possess special transportation and rescue units with medical teams, but they also provide training to the population for rendering aid to themselves and others. These units have special equipment caches that can be transferred quickly to a disaster site, and they are well furnished with individual and group communications systems.

In our country, such a service is only just beginning to come into being, even though it is in our country that the most serious mass disasters have occurred in the last five years. But it must be said that on the whole, the results of the provision of medical aid in these situations (not counting the Chernobyl accident) have been successful, owing to the colossal efforts and hard work of civilian and military institutions and to the enthusiasm of civilians and various specialists who exhibited very high mobility, dedication and true charity. International assistance from teams of rescuers and medical personnel and donations of equipment and medicines by state and public organizations, companies and private citizens of foreign countries played a definitive role as well. However, it must be said that our own efforts played the primary role, enabling us to begin providing first aid just hours after the disaster, and then to quickly evacuate casualties to specially prepared hospitals for qualified treatment.

For example, an hour after the earthquake in Armenia, 20 teams in ambulances from neighboring rayons were operating in the disaster regions. They were subsequently joined by 100 other such teams, including teams from adjacent rayons of Georgia. These teams provided first aid, which included use of basic antishock systems, immobilization of injured limbs, application of dressings and evacuation to the nearest intact medical institutions.

Within 24 hours, more than 1,200 physicians were working there, including 98 from Moscow, and as many as 10,000 hospital beds were set up within a radius of up to 100 km in intact hospitals in order to provide medical care to victims evacuated by air and ground transportation. In the first 24 hours, 130 airplane flights were made out of the earthquake region in order to evacuate victims to hospitals in Yerevan. A total of more than 5,000 Armenian physicians provided assistance to victims in the first 24 hours, and within two to three days, they were joined by at least 1,000 more physicians from Moscow, Leningrad, Kiev, Tbilisi, Rostov and other cities.

On 11 December (that is, on the fourth day after the earthquake), specialists began arriving from other countries (a total of 417 medical workers), and cargoes of medicines and medical equipment began coming in from 33 countries. Special mention should be made of the great assistance provided by the well-equipped and highly trained rescue teams from France and other Western countries.

Setting up surgical care during disasters is difficult not only because of the large number of people injured at the same time, the often poor access to the disaster site itself, and the destruction of local medical facilities, but also because information concerning the extent of damage and the number of injured is not always prompt or accurate. The inaccuracy of the information, resulting from the disruption of communications at the disaster site and from the obvious difficulty that the individuals providing the information have in quickly assessing the extent of damage and the number of victims, is often aggravated by the emotional trauma suffered by the informants themselves, who, in light of that, exaggerated or, just the opposite, understated the extent of the disaster. As a result, there may be a delay of one to two hours or more in mobilizing the regional medical service and especially the national medical service. In addition, the loss of this time substantially decreases the effectiveness of antishock and surgical aid rendered to the most seriously injured.

Even in the relatively minor disasters on railroads, in which 200-300 persons are injured, several hours pass before systematic medical aid begins to be rendered at the disaster site, despite the fact that large population centers are not far away. That time goes to assembling the medical workers, outfitting them with the necessary equipment, and delivering and deploying them to locations near the disaster site. Still more time is lost before aid—especially surgical aid and resuscitation—can be rendered to casualties in larger disasters that occur in regions that are far from major population centers and are inaccessible to transportation, as was the case in Armenia (Leninakan, etc.).

This is why we feel that the first action that must be taken is to quickly and objectively assess the nature and intensity of the affliction of the population and the number of casualties in the disaster, with consideration for the characteristics of the causal factor, geographic and climatic conditions, remoteness from medical centers and other circumstances. On the basis of those integral data, which are evaluated in the context of a program set up ahead of time on the basis of analyzed experience, strictly defined contingents of medical workers and equipment and the

closest medical institutions must be activated, transportation of medical personnel to the disaster site and the ways and means of evacuating casualties must be determined, and problems associated with coordination with other services supporting rescue and recovery operations must be solved.

Medical detachments from neighboring regions, republics and even the country's center arrived in the earthquake regions of Armenia in the first 3-12 hours, but at first, their equipment did not correspond fully to the working conditions. In the 24 hours, there were not enough tents for field operating rooms and hospital complexes, and there were few self-contained power and water supply sources, although the aviation component did work excellently, supporting the delivery of people and gear and the evacuation of casualties. Nonetheless, owing to the great organizational effort and the compassion felt for the victims by the entire nation, the system that was created in the first two to three days out of local and large, promptly arriving contingents of medical workers—primarily in the surgical specialties (general surgeons, anesthesiologist-resuscitation specialists, neurosurgeons, traumatologists)—made it possible to provide assistance to all 19,000 casualties, of whom almost 11,000 were hospitalized because of the severity of their injuries. Practically all seriously injured patients were quickly evacuated by air to large hospitals of Yerevan and other cities of the USSR in order that qualified surgical and resuscitation care could be provided.

News of the disaster compelled many medical workers and other specialists—both in our country and in other countries—to go to Armenia. This desire to help the victims—displayed by individual groups of people and public organizations, including a number of national Red Cross societies and a number of companies in Western countries—made a great contribution to the treatment and rehabilitation of the victims. Delivery of medical equipment and scarce medicines was of especial importance, since no single public health service from any one country is geared to instantaneous provision of assistance to such a large number of people with serious, usually multiple injuries complicated by dangerous wound infection and the crush syndrome and its sequelae.

The need for detoxication systems for patients with the crush syndrome—which was often complicated by fractures, purulent wounds, and other injuries—was especially great. Hemodialysis, plasmapheresis, hemosorption and ultrafiltration were employed. Foreign organizations and our own colleagues specializing in these procedures provided inestimable assistance in setting up a number of these procedures for mass use.

On the other hand, the number of volunteers that came to Armenia from different regions of the Soviet Union and from abroad was, in the final analysis, too large. A number of specialists were displeased by the lightness of their work load and by the difficult living conditions that stemmed from the clustering of the large number of people carrying out rescue and recovery operations.

Based on an analysis of the medical aid provided at a number of disasters, we are convinced that what is required is a carefully considered number of medical workers limited to what is objectively needed, plus enough equipment to support their work. For that purpose, the USSR Ministry of Health adopted a decision to create an all-union practical coordinating center for providing care to the public in major natural disasters and accidents. We feel that organizing a center that, as such, will enable us to have on-call medical teams (surgical and anesthesiological) with the appropriate gear for traveling to an accident site in constant readiness will substantially improve the timeliness and effectiveness of surgical aid provided to victims. This service will also be able to participate in providing assistance to other countries in major disasters.

We are learning much from our experience in providing medical aid to victims of the gas pipeline explosion at Ufa. As is known, two passenger trains carrying a total of around 1,500 passengers were involved in this disaster. Of the 1,224 individuals who were injured (burns primarily), 806 were hospitalized. This was done in a highly organized way, and quickly, owing to the efforts of local inhabitants and medical workers, and as a result of the enlistment of all available transportation resources, including military helicopter subunits. Patients were concentrated in many hospitals of the cities of Asha, Ufa, Chelyabinsk and others, where they were given qualified medical assistance on the very first day. Then, after the initiation of intensive care, the victims were concentrated in specialized burn centers of Ufa, Chelyabinsk, Kuybyshev, Moscow and other cities. A total of more than 78 percent of the hospitalized victims recovered. This is very high for such a large number of severe burn victims, the bulk of whom suffered injuries not only to extensive body surfaces, but also to the respiratory tract. This was the result of the selfless emergency work of local medical workers, public health organizers, volunteers, transportation workers and representatives of many government agencies, all of whom arrived at the disaster site quickly.

However, the experience associated with eliminating the medical consequences of these disasters and an analysis of the assistance rendered after the explosion in Arzamas also revealed a number of significant negative features. Primary among them is the delay in initiating antishock therapy at the accident site, which was the result of medical teams not being brought to the disaster site quick enough and their lack of infusion therapy equipment (the small quantity of systems for intravenous drop infusion and of the infusion media itself). Because metering units such as the Infuzomat are not part of the supplies, infusion therapy virtually ceases because of pressure gradients when casualties are transported by air.

One of the serious shortcomings revealed in surgical care was the fact that some surgeons did not pay enough attention to wound infection or local changes in tissue, especially where it underwent prolonged compression. As a result, excision of traumatized soft tissues was often relatively sparing, with minor scarification of the skin performed rather than dissection and excision of unviable tissues, and primary sutures were applied after amputations and primary surgical treatment of wounds. The latter

led to the advent of severe suppurative processes. The subsequent course of illness was typified in such cases by greater severity of condition of many surgical patients (on the 4th-6th days after injury) as a result of crush syndrome and progressing suppurative processes in wounds (going as far as development of typical nonclostridial and clostridial mixed anaerobic phlegmons and profound myositis, despite continuing intensive, massive antibacterial therapy). Repeated extensive surgical treatment of wounds, coupled with excision of large masses of unviable muscle and other tissues, and wide use of afferent treatment methods (hemosorption, plasmapheresis, hemodialysis) were required in this period.

We are convinced that inadequately extensive primary surgical treatment, even when subsequent active surgical treatment is done properly, is fraught with the danger of unfavorable outcomes. In such cases it becomes impossible to save a limb, and frequently life itself.

Nor has the advisability of "trouser-stripe" incisions for pronounced edema of limbs in crush syndrome been fully resolved yet. Some surgeons feel them to be necessary no matter what the stage of treatment, while others associate them with development of severe suppurative processes, while still others feel that prompt plasmapheresis prevents and relieves edema.

It should be noted in conclusion that the creation and operation of a consolidated national medical disaster service, one associated with similar national units in other countries, should ensure the quick dispatch of specially trained and equipped medical detachments formed ahead of time to a disaster site, and the activities of those detachments should be subordinated to a carefully substantiated, unified medical doctrine that defines the nature and volume of aid provided in each stage of evacuation and treatment.

Prolonged Crush Syndrome. Communication I. Etiology, Pathogenesis, Clinical Pattern

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[Article by G. N. Tsybulyak, Leningrad]

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[Text] Prolonged crush syndrome (PCS) is a unique form of traumatic pathology developing as a result of prolonged crushing (4-8 hours or more) of the soft tissues of limbs by heavy fragments of damaged buildings or structures, by chunks of rock, or by earth. Other names are used for it as well: prolonged compression syndrome, crushing syndrome, traumatic compression syndrome, and crush syndrome, as well as release [sindrom osvobozhdeniya] or recirculation syndrome. Strictly speaking, they cannot be said to be true synonyms; they are more like pathogenetic variations of traumatic toxicosis. With true PCS, the integrity of muscles and other soft tissues is disturbed, and bone fractures are present in most cases (around 65 percent). With prolonged compression syndrome, owing to uniform forced compression and prolonged blockage of regional circulation, ischemic damage to large muscle masses comes to the fore. The mechanism of instantaneous entry of toxic substances into the systemic bloodstream is observed after removal of a tourniquet (tourniquet shock) or recovery of a major vessel, or after limb replantation (recirculation syndrome, or resumption of blood flow). The term "revascularization" doesn't fit such situations, since morphological restoration (growth) of vessels is not observed in situations of this kind. The Russian word *krash*, or *krashing*, translated from the English means crushing or shattering, and it can be considered a true synonym of the term PCS. All of the listed terminological variations are combined under the general pathogenetic umbrella of traumatic toxicosis, which is also used as a synonym of PCS.[10] Another variety of traumatic toxicosis has had currency in recent years—syndrome of prolonged static compression of a limb under the weight of one's own body; it is encountered in alcohol and other intoxications and in comatose states of varying etiology, when the patient is unable to change his body position by himself over a period of many hours, leading to blockage of regional circulation.

Pathological effects of traumatic toxicosis were described in the beginning of the century by Calmers (1909) and during World War I by Frankenthal (1916) and Kuttner (1918).[10] Albuminuria resulting from crushing and "traumatic nephritis accompanied by hematuria" were described still earlier (Bossar, 1882; Silberstern, 1909). The French physician E. D. Quenu (1919) made a special study of toxicosis among the wounded during World War I, and concluding that it plays an important role in the origin of life-threatening disorders, he proposed the toxic theory of traumatic shock. However, it was not until the beginning of World War II, during treatment of the victims of the German bombing of London, that PCS was singled out as an independent pathology.[25-27]

In the USSR, this syndrome was first described by A. Ya. Pytel (1945). After the Ashkhabad earthquake of 1948, it was carefully studied by M. I. Kuzin.[9] The great importance of PCS to military medicine stems from the adoption of powerful explosive munitions (thermonuclear weapons, vacuum bombs) by modern armies. After atomic bombs were dropped on the Japanese cities of Hiroshima and Nagasaki in 1945, PCS was observed in 20 percent of the casualties, and it was accompanied by a high mortality rate—60 percent.[16] PCS is encountered in peacetime in mine cave-ins, in quarries, and in major transportation and industrial accidents, when people are crushed for long periods of time by rock, huge pieces of machinery, and building fragments. The significance of PCS grows especially during earthquakes. It is believed that in all of mankind's history, earthquakes have claimed at least 14 million lives.[16] Across the globe every year, there are as many as 25 major earthquakes in which approximately 1 megaton of energy is released, which is equivalent to the explosion of 50 of the atomic bombs dropped on Hiroshima and Nagasaki in 1945. In earthquakes, PCS is found in 3.5-5 percent of all victims; crushing of the lower limbs occurs more often (79.9 percent) than of the upper

limbs (14 percent); simultaneous injury of upper and lower limbs is recorded in 6.1 percent of the cases.[10] Among the casualties of the especially strong earthquake in Armenia, PCS was noted in 23.9 percent of all victims.[15]

According to modern views, two mechanisms can be distinguished in the etiology and pathogenesis of PCS—forcible compression of large masses of tissue, coupled with their prolonged ischemia, and direct damage to anatomical structures of the closed or open type. The pathological consequences *per se* of direct damage to cells manifests itself right away, while in the presence of ischemic injury to muscles it is observed several hours later. Because the average time before ischemic death of striated musculature is around six hours, it would be logical to assume that the mechanical factor is the cause of early necrosis (in the first hours), while hypoxia assumes importance later on.[29] As a result of direct destruction of tissues, intracellular substances (lysosomes, mitochondria etc.) enter the blood; in the case of compressive-ischemic injury of muscles, it is mainly "ischemic substances" (acid metabolites of anaerobic glycolysis) that accumulate and enter the systemic circulation. In both variants, circulatory and respiratory disorders arise, but the symptoms increase more slowly in response to "ischemic toxins." Cases of rapid death after a relatively short-term action of the traumatizing agent is attributed to preferential destruction of muscles.[29] Consequently, a direct parallel does not exist between the extent of injury and the time of traumatizing action, on one hand, and the degree of expression of the clinical manifestations of PCS, on the other, inasmuch as the nature of injury has great significance. An increase in the blood (and urine) creatine/creatinine index is typical of irreversible tissue destruction brought about by mechanical damage; this index can serve as an objective criterion in answering the question as to early amputation of a limb.[29] Prolonged ischemia makes PCS similar to tourniquet shock and other conditions associated with resumption of regional circulation (restoration of blood flow in a major vessel, replantation of a limb). In PCS, circulation is disturbed not only in the arteries but also in the veins, where thrombosis and impairment of the contractility of vessels are observed.[3] As a result of profound ischemia of muscles, ATP begins to break down, carbohydrate and fat metabolism is disturbed, and lactic acid and other metabolites accumulate in the blood. The fact that a larger part of the myoglobin (75 percent), potassium (60 percent), phosphorus (75 percent) and acid metabolites (95 percent) are released from compressed muscles was established back in the first studies on PCS.[25-27] In the course of subsequent decompression, not all researchers detected resumption of microcirculation in injured muscles, whose vessels are found to exhibit profound morphological changes, as is true of cells outside them as well.[22] It was established in experiments on animals that destructive-degenerative changes develop in the nervous formations of injured muscles in the first few minutes after compression.[22] Substances that determine the state of traumatic toxicosis include the products of protein breakdown, histamine, serotonin, bradykinin, creatinine, and ATP derivatives—adenosine and adenylic acid. The blood aldolase level rises, which can serve as an objective criterion by which to make conclusions concerning the scale of injury, and the final prognosis; at the same time, growth of the levels of CPK [creatine phosphokinase], LAD_4, LAD_5 (due to injury of striated muscles and the heart) bring about hyperenzymemia.[23] However, myoglobinemia plays the leading role in the mechanisms of pathological disorders accompanying PCS. Myoglobin obturates small vessels in the lungs, liver, kidneys and other internal organs.

It is retained for a long time in the vascular lumen, which is responsible for intoxication of the organism and serves as the basis for development of severe complications (acute renal insufficiency—ARI, acute hepatic insufficiency, abscessing pneumonia), often with a lethal outcome. Decomposition of striated muscles (rhabdomyolysis) and accumulation of myoglobin, potassium, phosphorous, uric acid, lactate and other acid products in the blood leads to development of metabolic acidosis. In the presence of acidosis, myoglobin is transformed into hydrochloric hematin, which directly obturates the ascending limb of Henle's loop and evokes inflammatory-degenerative changes in the tubular epithelium, going as far as its necrosis. ARI often develops (in 50 percent of the cases) against the backdrop of developing hypoxemia, arterial hypotension and reflex spasm of vessels in the cortical layer of the kidneys. Acute blockage of the kidneys against the backdrop of PCS carries a less favorable prognosis than their blockage in the presence of other pathological states accompanied by hemolysis and myoglobinuria.[28] However, precisely what the direct cause is of PCS in prolonged crushing—mechanical obturation of canaliculi, or the toxic effects of myoglobin, or hematin, or necrotic tubular epithelium—has not yet been clearly determined. The possibility is not excluded that the vasomotor phenomenon—that is, spasm of afferent arterioles, arising in renal glomeruli in response to myoglobin and its catabolites—plays the decisive role. The opinion exists that microthrombi, globules of de-emulsified fat, and, beginning 24 hours after the injury, hematin evoke obturation of afferent arteries and glomerular capillaries. Toxins and proteolytic enzymes circulating in the blood damage the endothelia of glomerular capillaries, Bowman's capsules and the basal membrane of canaliculi, resulting in penetration of formed blood elements into urine.[15] Disturbance of renal function is recorded in animal experiments beginning in the first few minutes of compression (a neuroreflexive effect); in the decompression period, functional insufficiency of all segments of the nephron grows even more, and disseminated intravascular coagulation arises in the kidneys.[20] As a result of disturbance of carbohydrate metabolism, in the kidneys the concentration of glucose and uric acid rises and the activity of hexose monophosphate changes.[14] Special emphasis should be laid on the fact that acidotic changes in urine represent the most important pathogenic factor responsible for damage to renal canaliculi and development of ARI. For example, intravenous injection of hemo- or myoglobin into animals elicits ARI only when the pH of urine is below 6.0; at a higher pH, ARI does not develop.[24] The more extensive the zone of muscle compression or

ischemia and the longer the duration of the traumatic effect, the more severe is the course of ARI.[10]

As with the kidneys, the liver is not injured directly in PCS, but it is included in the development of the pathological process from the very first stages of injury. Evidence of this can be found in particular in activation of the lysosome apparatus in the cells of these organs prior to development of toxemia.[6] In experiments on dogs, compression of the hind limbs slowed renal circulation and elicited dystrophic changes in hepatocytes and depletion of the carbohydrate and protein reserves in the organ.[13] Profound morphological changes disturbing regional hemodynamics and organ function are observed in hepatic vessels in PCS.[1] After crushing, liver function may be inhibited for many months and even years.[18] Destructive-degenerative changes promoting development of toxemia and inhibition of immune status and regenerative processes are observed in hepatocytes, cells of the reticuloendothelial system, and hepatic macrophages in experimental morphological study.[18] Foci of micronecroses are observed in the livers of experimental animals during the decompression period.[1] The pronounced therapeutic efficacy of hooking up an artificial liver, which helps to relieve shock and prevent development of ARI, confirms the important role played by liver dysfunction in PCS.[8,11] According to polarographic analysis of PaO_2, the liver and muscles are the organs and tissues most sensitive to prolonged crushing of limbs; the brain is rather resistant, but circulatory hypoxia arising in it can be associated with profound disturbances of hemodynamics.[7]

Massive loss of plasma is an important factor in the pathogenesis of disturbances of vitally important functions accompanying PCS. Plasma loss due to tissue edema attains 3-4.7 percent of body weight, according to experimental studies—that is, more than 30 percent of the volume of circulating blood.[10] Loss of large volumes of plasma occurs as a result of disturbance of the membrane permeability of the endothelium of vessels in traumatized muscles, which itself leads to serious disturbance of hemodynamics and worsening of hypoxia, but it does not at all entirely explain the severity of functional disorders.[5] Restoration of the volume of circulating blood and normalization of fluid spaces are not enough in themselves to stabilize circulation and respiration; this fact confirms the important pathogenic role played by toxic effects.[29] Reduction of cardiac ejection is recorded in animal experiments in the compression period; it increases quickly after decompression.[2] With plasma loss, hemoconcentration, reduction of the chemical and osmotic resistance of erythrocytes, intravascular hemolysis and anemia increase, and erythropoiesis is inhibited; there is diagnostic and prognostic significance to determining the level of myoglobinemia and erythrocyte resistance.[19] In PCS, blood coagulation accelerates, recalcification time and the level of free heparin decrease, and the plasma heparin-tolerance and fibrinogen-concentration rise.[12] Hypercoagulation is associated primarily with massive entry of thromboplastic substances into blood from the zone of damaged tissues. Plasma loss and hemoconcentration—that is, growth of the concentration of formed elements per unit blood volume—and growth of blood coagulability and viscosity worsen the rheological (flow) properties of blood.[17]

Morphological changes have been studied in detail with an experimental model of PCS[21]: in nerve cells, dystrophic changes are noted; in lungs, acute stagnant plethora and areas of atelectasis, dysatelectasis, hemorrhage and emphysema; in the heart, anoxic changes, circulatory disorders, foci of acute damage and degeneration; in adrenal glands, acute dystrophic and necrobiotic processes against the backdrop of circulatory disorders and hemorrhagic diathesis; in the adrenal cortex, dystrophic processes and foci of segmental necroses; in the hypophysis, circulatory disturbances; and in the posterior lobe of the hypophysis, disappearance of neurosecretin and mycoid granules; in traumatized muscles, an irregular nature of injury, areas of waxy necrosis, and total infiltration with highly serous inflammatory exudate. Postmortem examination of people who died of PCS reveals edema of subcutaneous fat and muscles and foci of imbibition with blood in the zone of injury, with normal muscle tissue alternating with foci of its necrosis; hemorrhages are revealed in perineuria and in vascular adventitia; coagulational necrosis is visible microscopically in crushed muscle tissue; lungs are edemic and plethoric, organs of the abdominal cavity are plethoric, with hemorrhage into the mucous membranes of the stomach, duodenum and the initial and terminal divisions of the small intestine; kidneys are of normal size or slightly enlarged, their cortical matter is dry and pale yellow, while their medullar matter is plethoric and dark red, and changes typical of acute toxic-infectious injury (arising in massive hemolysis, dehydration and intoxication) are microscopically visible.[10]

Thus, direct mechanical injury, as well as ischemic injury, of muscles plays the decisive role in the pathogenesis of PCS. Plasma loss, hypovolemia, hemoconcentration and the hemodynamic disorders associated with these conditions, as well as acute organ pathology—primarily affliction of the kidneys and the liver—are of no small significance. Pain and negative neuroreflexive effects doubtless play a role in forming pathological responses, especially in the early stages of PCS. Prolonged (more than eight hours) crushing of the limbs of animals which had their spinal cord cut three to seven days prior to this (to deactivate reactions to painful stimulation) proceeds noticeably more mildly than in intact animals.[10] It has already been noted that prolonged painful stimulation elicits spasm of vessels in the cortical matter of the kidneys and restriction of glomerular filtration; renal circulation proceeds under such conditions primarily by way of vessels of the medullar substance.[10]

A knowledge of the mechanisms of the development of PCS makes it possible to establish its working classification. That classification takes into account the type of traumatic effect (crushing, compression, static compression, their combination); severity (mild, moderate, severe); accompanying injuries (to bones, vessels, nerves, internal organs); arising complications (renal insufficiency, hepatorenal insufficiency, suppurative-infectious complications,

ischemic complications, etc.).[15] Such a classification helps to maximally individualize treatment and to make it purposeful and optimal.

The clinical pattern and severity of PCS are determined by the nature and scale of injury, the force and duration of the traumatic effect, and the degree and time of blockage of regional circulation. According to the classical description, severe PCS is typified by a general pattern of deep shock, induration, edema and insensitivity of traumatized muscles, and reduction of their temperature; oligoanuria arises after several hours or days as a consequence of ARI developing against the backdrop of myoglobinemia and tubulo-interstitial nephropathy.[25-27] Most researchers feel that crushing of one entire limb for six hours is crucial to the development of PCS. However, in the opinion of a number of authoritative researchers of the problem, crushing of 50 percent of a lower limb for more than four hours is enough to predetermine a severe course for the syndrome; a lesser area and shorter time of crushing also elicit forms of PCS of lesser severity.[10] Extremely severe forms develop after intensive crushing of two or more limbs or substantial portions of the body for eight hours or more; a lethal outcome occurs within the first one or two days. However, numerical criteria for the area and duration of crushing in PCS are purely preliminary, and they cannot serve as a dependable basis for prognosis, inasmuch as the nature itself of the injury and concomitant damage to bones, vessels, nerves and internal organs predetermine a great deal.

In the first few hours after victims are removed from debris, they complain of pain and impaired movement in the joints of a damaged limb. Hypothesia or anesthesia, absence of articular reflexes, and mild paralysis (partial, complete) are noted locally. However, the overall condition may remain stable over the course of a certain amount of time. Later, weakness, dizziness, sluggishness, nausea, pale skin, cold sweat and tachycardia set in. The traumatized limb is edemic and cyanotic, it is covered by abrasions and hemorrhages, and pulsation of peripheral vessels within it is weak. Edema attains its peak within 12-24 hours, which is when inflammatory reddening, blisters and vesicular rashes arise as well. In the absence of peripheral pulsation, damage to the main artery can be averted by means of dopplerography.[30] The very first portions of urine acquire a dark brown color (myo- and hemoglobinuria); there is a great deal of protein in urine (6-12 percent), while sediment contains cylinders and cylindrical objects resembling casts of convoluted canaliculi containing desquamated epithelium, chunks of amorphous myoglobin, and hematin crystals. Initial alkalosis is superseded by progressive acidosis. Even with accompanying blood loss, blood analyses reveal a high concentration of hemoglobin, a high hematocrit and a large number of erythrocytes (hemoconcentration); whereas analysis of the biochemical composition of blood reveals an increase in levels of nitrogenous residues (residual nitrogen, urea, creatinine), potassium and phosphorus. Increasing bilirubinemia and elevation of the concentration of enzymes in blood (alkaline phosphatase, CPK, AST, ALT, LAD) are evidence of the addition of acute hepatic insufficiency.

Three periods can be discerned in the dynamics of PCS: early, with shock phenomena dominating (up to day three after injury); intermediate, determined by signs of ARI (from day three to days 8-12); late, or recovery (from the beginning of the second week to one to two months).[10]

Dramatic worsening is observed in the course of the pathological process right away or soon after the compressed limb is freed, which is associated with massive entry of toxic substances into the systemic circulation. It is in the first few minutes of decompression that a sharp rise in the concentration of potassium, enzymes and products of cell autolysis is recorded. In the shock period, circulatory disturbances dominated by vascular insufficiency are maximally expressed. Shock accompanies only the severe forms of PCS, and it is characterized by pain, mental and emotional stress, and growing hypovolemia and hemoconcentration. Edema and woody induration of the limb are noted locally. Intensive care started early makes it possible to get the patient out of his serious condition; when treatment is inadequate or late, death may occur early. After the patient recovers from shock, an intermediate, or lucid, period sets in. It is also observed in the most severe forms accompanied by a lethal outcome. The condition of patients gradually improves, pain abates, arterial pressure returns to normal, pulse slows, and temperature is elevated to 37.5-38.5°C; oligoanuria is observed as before. Hyperkalemia, hyperphosphatemia and hypercoagulation persist, and, as before, an elevated concentration of residual nitrogen, urea and creatinine is determined in blood. The next period of PCS manifests itself on the fourth or fifth day after injury with signs of ARI (dyshidrosis, hyperazotemia, hyperkalemia, and growing metabolic acidosis). Diuresis decreases to a critical level (40-20 ml/hr); apathy, anorexia, nausea and vomiting progress. Blood analysis reveals anemia, hyponatremia, hypocalcemia and a reduced protein concentration—5.9 + 0.1 gm-percent.[4] ARI may also develop in patients who had not previously suffered shock.[10] Foci of necrosis form locally in this period in the zone of greatest compression, and sloughing of dead skin and underlying tissues results in formation of wounds, coupled with their possible infection and development of phlegmons. In the final recovery period, the function of the kidneys and other internal organs is gradually restored, the water-electrolyte balance returns to normal, and edema of the injured limb disappears completely. Local changes manifest themselves as muscular atrophy, contractures and stiffness of joints. Burning pains recalling causalgia, documented in more than half of victims with damage to upper limbs and in about a third of victims with damage to lower limbs, may arise in connection with development of ischemic nephritis.[10]

References

1. Arbuzova, E. Ye., in "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey" [Targeted Treatment of Severe Traumatic Ischemia of the Limbs], Kemerovo, 1978, pp 29-31.

2. Bukov, V. A. and Zairov, D. K., in "Aktualnyye problemy sovremennoy patofiziologii" [Urgent Problems of Modern Pathophysiology], Kiev, 1981, pp 63-65.

3. Gaisin, A. G., in "Profilaktika proizvodstvennogo travmatizma v rayonakh dobychi nefti" [Prevention of On-the-Job Trauma in Oil Drilling Regions], Tyumen, 1978, pp 180-182.

4. Goryachev, A. N. and Turishcheva, I. G., in "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 72-75.

5. Isayev, M. R., Korneyev, A. A. and Kravtsova, V. A., VESTN. KHIR., No 8, 1980, pp 125-128.

6. Kobylyanskiy, L. N., ZDRAVOOKHRANENIYE. KISHINEV, No 5, 1986, pp 39-41.

7. Kravtsov, V. V., PAT. FIZIOL., No 6, 1975, pp 17-22.

8. Krichevskiy, A. L., in "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 11-14.

9. Kuzin, M. I., "Klinika, patogenez i lecheniye sindroma dlitelnogo razdavlivaniya: (Travmaticheskiy toksikoz. krash-sindrom)" [Clinical Pattern, Pathogenesis and Treatment of the Prolonged Crush Syndrome: (Traumatic Toxicosis, Crush Syndrome)], Moscow, 1959.

10. Kuzin, M. I., "BME" [Great Medical Encyclopedia], 3d edition, Vol 5, Moscow, 1985, pp 188-190.

11. Kuzin, M. I., Sorokina, M. I., Troynyakov, N. K. et al., in "Osnovopolozhniki sovetskoy voyenno-polevoy khirurgii" [Founders of Soviet Military Field Surgery], Moscow, 1976, pp 31-33.

12. Kurbatova, Z. A., in "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 23-26.

13. Lopatin, A. G., "State of the Liver in the Early Period of the Prolonged Crush Syndrome and Assessment of the Methods of Sanitation of a Traumatized Limb": Abstract of a dissertation in pursuit of the academic degree of candidate of medical sciences, Moscow, 1981.

14. Nesterenko, G. I., PAT. FIZIOL., No 2, 1978, pp 54-59.

15. Nechayev, E. A., Lizanets, M. N., Bryusov, P. G. et al., VOYEN.-MED. ZHURN., No 4, 1989, pp 11-14.

16. Nigulyanu, V. I., Yelskiy, V. N., Krivoruchko, B. I. et al., "Sindrom dlitelnogo razdavlivaniya" [Prolonged Crush Syndrome], Kishinev, 1984.

17. Savitskiy, G. G., Revskoy, A. K., Rybin, S. A. et al., in "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 32-34.

18. Sekamova, S. M. and Beketova, T. P., BYUL. EKSPER. BIOL., No 11, 1985, pp 614-617.

19. Timoshchuk, G. I., in "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 27-29.

20. Troynyakov, N. K., in "Aktualnyye voprosy sovremennoy khirurgii" [Urgent Problems of Modern Surgery], Moscow, 1977, pp 121-123.

21. Shakul, V. A., Imerekov, G. A., Golovin, V. S. and Lopatin, A. G., in "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 14-19.

22. Shilnikov, G. V. and Churilov, Yu. S., in "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 20-23.

23. Chernikova, L. M. and Shepotinovskiy, V. I., PAT. FIZIOL. , No 4, 1985, pp 23-29.

24. Bursztein, S., "Annual Symposium on Critical Medicine, 23d: Proceedings," Las Vegas, 1985, pp 497-499.

25. Bywaters, E. and Beal, D., BRIT. MED. J., Vol 1, 1941, p 427.

26. Bywaters, E., Delory, G. et al., BIOCHEM. J., Vol 35, 1941, p 1164.

27. Bywaters, E., BRIT. MED. J., Vol 2, 1942, pp 643-646.

28. Michatson, M., Taitelman, U. and Bursztein, S., RESUSCITATION, Vol 12 No 2, 1984, pp 141-146.

29. Santangelo, M., Usberti, M. et al., SURG. GYNEC. OBSTET., Vol 154 No 3, 1982, pp 372-374.

30. Tsherne, H., LANGENBECK ARCH. CHIR., Vol 358, 1982, pp 243-244.

Organization and Tactics of Specialized Medical Aid in Mass Poisonings

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[Text] Acute mass poisonings are said to be one of the typical emergency situations encountered by emergency medicine every year in various countries. Such poisonings are most likely in regions or population centers with concentrations of chemical enterprises that use various strong-acting toxic materials in their production, as well as railroad junctions, industrial cold-storage warehouses, meat packing plants and water treatment facilities.[1] Mass poisonings involve a sizable number of victims (from several dozen to several thousand persons). The methylisocyanate poisoning in Bhopal, India, where the victims numbered several thousand, is the largest in recent years.[2] Fortunately, such disasters are rare, but even when the number of victims is considerably lower (around 100), organizing emergency medical aid is a rather complex task. Major disasters involving a large number of victims must be responded to with the participation of civil defense resources and with the quick-response medical service being created in our country. To date, however, all medical aid, including specialized aid, has been rendered to victims of mass poisonings by ordinary treatment-and-preventive facilities. The term *specialized medical aid in mass poisonings* is taken to

mean the hospital stage of treatment of victims in a specialized toxicological center or in a general hospital under the observation of a consulting toxicologist, where the necessary examination and treatment can be conducted at the level of the requirements of a specialized toxicology department.

This paper presents the experience of the All-Union Acute Poison Treatment Center in rendering medical aid in 25 cases of different mass poisonings over the last 11 years. The structure of these poisonings is shown in Table 1.

Table 1. Structure of Acute Mass Poisonings According to Data of the All-Union Poison Treatment Center for 1979-1989

Year	City or Other Population Center	Name or Source of Poison	Route of Poison's Entry Into Body	Cause of Poisoning
1979	Tyumen	Methanol	Peroral	Consumed for alcoholic intoxication
1980	Kemerovo	Cellosolve	Peroral	Consumed for alcoholic intoxication
1980	Pedzhikent	Karakurta toxin	Bite	Massive bites among kishlak population by spiders
1981	Fishing vessel	Sigvatera	Peroral	Consumption of contaminated fish
1982	Tashkent	Poisonous mushrooms	Peroral	Consumption as food
1983	Groznyy	Sulfuric acid	Inhalation	Violation of production procedure
1983	Orsk	Sodium silicofluoride	Peroral	Poison accidentally mixed with food
1984	Kurgan	Polyisocyanate	Inhalation	Violation of production procedure
1984	Novosibirsk	Yuksovsko-Sartlanskaya disease	Peroral	Consumption of contaminated fish
1984	Novgorod	Cellosolve	Peroral	Consumed for alcoholic intoxication
1985	Volgodonsk	Poisonous mushrooms	Peroral	Consumed as food
1985	Moscow	Methanol	Peroral	Consumed for alcoholic intoxication
1986	Murom	Cellosolve	Peroral	Consumed for alcoholic intoxication
1986	Kursk	Organophosphorous and organochloride pesticides	Inhalation	Industrial safety violation
1986	Novodvinsk	Methanol	Peroral	Consumed for alcoholic intoxication
1987	Saratov	Poisonous mushrooms	Peroral	Consumed as food
1987	Cheboksary	Methanol	Peroral	Consumed for alcoholic intoxication
1988	Rostov-na-Donu	Mercury	Inhalation	Violation of mercury-instrument operating rules at work
1988	Gorkiy	Methanol	Peroral	Consumed for alcoholic intoxication
1988	Surgut	Carbon monoxide + respiratory tract burns	Inhalation	Aircraft accident fire
1988	Ivanovo	Ammonia	Inhalation	Motor transportation accident
1989	Orenburg	Hydrocarbons, mercaptans	Inhalation	Population poisoned by discharge from gas refinery
1989	Sverdlovsk	Sumitsidin, tsimbush	Inhalation + transcutaneous	Violation of rules for using insecticides in agriculture
1989	Donetsk	Chlorobenzene	Inhalation + transcutaneous	Industrial accident

In terms of cause, the poisonings were either industrial (seven cases, or 28.0 percent) and household (18 cases, or 72.0 percent). The main causes of the mass industrial poisonings were, as a rule, either procedural violations or failure to observe industrial safety practices. Among the household causes, most poisonings were due to consumption of toxic materials in order to achieve alcoholic intoxication (seven cases) and consumption of toxic materials with food (food poisoning, six cases). The other poisonings are also of a certain amount of interest, since they reveal the diversity of situations that lead to mass poisonings: carbon monoxide poisoning by a fire in an airplane (aircraft accident), poisoning by gas refinery products, and massive bites by poisonous spiders.

The mechanism of the poison's entry into the body was either inhalation (10 cases, or 40.0 percent)—including two cases of combined inhalational and transcutaneous entry—or peroral (14 cases, or 56.0 percent). The one case of entry of poison by spider bites may be considered as an injection route. When we compare the characteristics of poisonings with respect to toxin entry routes and causes of poisoning, we find the following: industrial inhalation, seven; household inhalation, three; peroral, 14.

It is evident from Table 1 that the pathology associated with the industrial poisonings group involves substances with a predominantly irritating, burning action and, to a lesser degree, substances with a general toxic action; the

household poisonings group is dominated by substances of general toxic action (methanol, ethylene glycol ethers) and hepatonephrotoxic action (poisonous mushrooms, Yuksovsko-Sartlanskaya [transliteration] disease). Our analysis enables us to determine the principal pathological syndromes in these poisoning groups: respiratory disorders, disrupted hemodynamics, injury to the nervous system, injury to the gastrointestinal tract, and injury to the liver and kidneys. The number of victims of these mass poisonings was 20-200 persons, with the greatest frequency of cases with a large number of victims (60-200 persons) in the inhalational poisoning group. Lethal outcomes were not noted in all cases. For example, in the mushroom poisonings and in most inhalational poisonings, there were either no lethal outcomes or just a few. In the methanol and ethylene glycol poisonings, lethal outcomes were observed in practically every case of mass poisoning, and the percentage of deaths was 10-30 percent.

In cases of mass poisoning, the consulting toxicologist must carry out the following tasks: (1) make the diagnosis of acute poisoning, including refining and confirming the diagnosis of local specialists, and carry out differential diagnosis of poisonings accompanied by other diseases; (2) determine the direction and volume of special and clinical examination of victims; (3) develop the complex of therapeutic measures and provide practical assistance in their organization; (4) evaluate the prognosis, complications and outcomes of poisoning, determine more specifically the toxicological danger of the situation jointly with other specialists, and take part in the development of preventive measures; (5) evaluate the diagnostic, therapeutic and organizational work of local specialists and evaluate recommendations.

Diagnosis of mass illnesses begins with isolating one or several leading syndromes or symptoms that are typical of most of the victims, which would make it possible first of all to confirm the suspicion of acute poisoning and to determine the nature of action of the toxic material in accordance with the principle of "selective toxicity" of poisons. In particular, the most characteristic early symptoms of inhalational poisoning by ammonia, strong acid vapors, polyisocyanate and mercury vapors are injurious to the mucous membranes of the eyes, nose and pharynx, and respiratory tract (from mild irritation to toxic tracheobronchitis and pulmonary edema). When poisons of general toxic action are inhaled (carbon monoxide, chlorobenzene, hydrocarbons), narcotic action upon the central nervous system assumes the forefront. Similar tactics for isolating the leading symptoms are used when diagnosing peroral poisonings, particularly by alcohol surrogates (methanol, ethylene glycol ethers)—in which the narcotic effect of the poisons is the earliest manifestation (sopor, coma, encephalopathy)—and by poisonous mushrooms, which often bring on toxic gastroenteritis. It should be noted that other symptoms (injury to the liver, kidneys and the peripheral and autonomic nervous system) develop later—on the second or third day, and they can also be used as data confirming the preliminary diagnosis.

Laboratory chemical-toxicological diagnosis, which is aimed at detecting the toxic substance in the blood and in the body's other biological media, is used in such cases rather rarely in view of the toxicokinetic and physicochemical properties of the poisons. For example, it is practically impossible to detect poison in the blood in the case of poisoning by acid vapors, ammonium vapors, or chlorine vapors or hydrocarbons, mercaptans, or mushroom toxins. In other cases (methanol, ethylene glycol, mercury), the presence of the poisons can be determined, and methods of quick analysis have been developed and can be conducted with Soviet-made apparatus. Biochemical analyses are also used for diagnostic purposes: the test for acid-base balance is successful as a means to determine carboxyhemoglobin, methemoglobin, and blood cholinesterase activity, and to diagnose poisoning by ethylene glycol and its ethers and methanol.

To make an emergency diagnosis, it is sufficient to examine 10-15 patients with the same clinical pattern of injury. During treatment, it is advisable to subject all patients to chemical-toxicological and biochemical tests in order to determine the severity of injury and to evaluate the effectiveness of treatment. Moreover, beginning with the second or third day, it is necessary to analyze liver and kidney function and blood composition, especially in cases of poisoning by hepato-, nephro- or hemotoxic substances. Besides those listed above, other emergency analyses include x-ray analysis of the lungs—in the cases of poisoning by gases with irritating, burning and suffocating action, and bronchoscopy—when such poisoning is accompanied by thermal burning of the respiratory tract. When poisoning involves hepato- and nephrotoxic poisons, it is advisable to carry out radionuclide hepato- and renography. Diagnostic laboratory and instrumental analyses recommended in relation to different types of mass poisonings are presented in Table 2.

Table 2. Diagnostic Laboratory and Instrumental Analyses Most Frequently Employed in Mass Poisonings

	Analyses of Blood, Urine						Instrumental Analyses	
Type of Poisoning	Chemical-Toxicological	Special Biochemical	Acid-Base Balance	Determination of Hematocrit Index	Clinical Blood Analysis	Biochemical Liver, Kidney Analyses	Lung X-Ray Analysis	Radionuclide Hepato- and Renography
Gases with burning and irritating action	-	-	+	+	+	-	+	-
Mercury	+	-	-	-	-	+	+	+
Chlorobenzene	+	-	-	-	+	+	+	+
Carbon monoxide	-	Determination of carboxyhemoglobin	+	-	-	-	+	-
Organophosphoric insecticides	+	Determination of acetycholinesterase in blood	-	-	-	-	-	-
Methanol	+	Acid-base balance	+	-	-	+	-	-
Ethylene glycol and its ethers	+	Acid-base balance, oxalates in urine	+	-	-	+	-	
Mushrooms	+	-	-	-	+	+	-	+
Food poisonings	When chemical agent is suspected	+ bacteriological analyses	+	-	+	+	+	+

Note: Here and in Table 3: "+" = diagnostic analysis mandatory, " + " = desirable, and "-" = not mandatory

Chemical-toxicological analysis of air, water, soil and suspected foodstuffs and beverages is a necessary and important supplement to clinical and laboratory diagnosis. These analyses are conducted by chemical-toxicological and bacteriological laboratories of sanitary-epidemiological stations (laboratories of various enterprises, scientific research institutes, etc., may be enlisted) also on the basis of the clinical pattern of poisoning, the chemical situation at the enterprise where the poisoning occurred and the ecological situation in the territory where the poisoning occurred. As a rule, however, these analyses are several hours to several days behind clinical analyses.

When deaths occur, data from autopsies also acquire diagnostic value, since they make it possible to reveal the most typical injuries of organs.

Victims are hospitalized on the basis of severity of poisoning (mild, moderately severe, severe). Patients with mild poisoning are hospitalized, as a rule, in therapeutic departments, or some are treated as outpatients. Patients suffering moderately severe and severe poisoning are admitted to a poison treatment center or to an intensive care-and-resuscitation department. For example, when poisoning is the result of poisons having irritating and suffocating action, persons with minimum manifestations taking the form of conjunctivitis and rhinitis are said to be mildly injured; moderately severe injury is diagnosed in persons with symptoms of tracheitis and tracheobronchitis without signs of respiratory or cardiovascular insufficiency; persons with signs of incipient or pronounced pulmonary edema, as well as with severe manifestations of aggravation of somatic diseases (stenocardia, myocardial infarct, and so on) against the backdrop of nonsevere poisoning, are said to be severely injured. The poison treatment center can carefully analyze each case and perform clinical toxicometry, comprehensive detoxication, and prognosis of outcomes in various age groups. All data obtained from examining the patients may be fed into the toxicological data bank of the All-Union Poison Treatment Center and may be used when necessary for consultative purposes in other treatment institutions.

As a rule, treatment at the place of an accident and upon admission to the hospital comprises general, basic elements, depending on the severity of the condition of the poisoned patients. Later on in a specialized hospital, the treatment process is individualized on the basis of laboratory data, the age of the patient, and other factors. One of the important areas of treatment is specific pharmacotherapy for poisonings, which includes administration of antidotes and drugs affecting the mechanism of the pathological process. It should be noted that antidotes may be of limited use in clinical toxicology; they may be employed in

10-15 percent of poisonings (organophosphoric compounds, metal compounds, ethylene glycol, and so on). In some cases (carbon monoxide) the most effective means of antidote therapy is hyperbaric oxygenation. Mobile pressure chambers are used for this procedure at the accident site or in a hospital that does not have a department with a pressure chamber. Antidotes are not used in poisonings by gases with suffocating, irritating and burning action; corticosteroids (hydrocortizone, prednisolone), administered parenterally in large doses and by inhalation in combination with broncholytic drugs, perform the role of specific therapeutic drugs. This is a very important method of pathogenic treatment that promotes improvement of external respiratory function and helps prevent pneumonia. However, providing enough inhalers to patients is a problem for hospitals, because as many as two-thirds of the victims require such treatment (practically all patients with moderately severe and severe poisonings).

The need for artificial respiration arises more rarely. In our observations, these are isolated cases, possibly because we have been dealing primarily with mild forms of intoxication. We should not forget, however, that cyanotic or gray hypoxia may develop as a result of chlorine poisoning, in which case conventional therapeutic methods must be supplemented by artificial respiration and by inhalation of oxygen together with a foam suppressor. The proper quantity of oxygen per patient is cited in the appropriate manuals. It should, however, be noted that in cases of mild and moderately severe poisonings by substances with suffocating and burning action (chlorine especially) with no phenomena of respiratory hypoxia, oxygen is not administered. In the case of poisoning by toxins with narcotic action, carbon monoxide, or alcohol surrogates, the need for artificial respiration is greater, and it may be required by (according to our observations) as many as 25-30 percent of the total number of victims, but most often, 5-10 percent.

Correction of hemodynamics and homeostasis is one of the subdivisions of symptomatic therapy requiring examination. Hemodynamic disturbances are assessed in most cases as exotoxic shock, and they correlate with the general severity of chemical trauma. Shock is treated by intravenous administration of various solutions. In light of this, treatment institutions must be provided with enough disposable systems and plasma-substitute solutions to provide treatment to all patients with severe or moderately severe poisoning for a period of three days. Severe decompensated metabolic acidosis is a unique feature of disturbances in homeostasis, observed in particular in poisoning by methanol and ethylene glycol and its ethers; its correction requires an average of up to 900-1,200 ml of 4 percent sodium hydrocarbonate solution per patient (it is better to have an 8 percent solution).

Emergency medical aid for acute poisonings includes detoxifying the body. This pertains primarily to substances with general toxic action. Forced diuresis is commonly accepted; however, success may be attained in certain types of poisoning only when it is combined with artificial detoxication—hemodialysis and hemosorption. In our observations, hemodialysis and hemosorption were conducted in response to poisoning by methanol, cellosolve, poisonous mushrooms and Yuksovsko-Sartlanskaya disease. The need for artificial detoxication methods may be 10-40 percent, depending on the number of severely injured victims of poisoning by alcohol surrogates. Given the length of one hemodialysis session (around six to eight hours), one "artificial kidney" unit can provide assistance to three patients a day. Thus, in order to ensure prompt hemodialysis (as patients are admitted and indications for it are revealed), at least five one-patient units or one SGD-8 multipatient "artificial kidney" must be available. In their practical work, toxicological centers have at times needed to enlist the help of the appropriate departments of other hospitals (oblast hospitals, as a rule) in conducting hemodialysis by transferring some of the patients requiring hemodialysis and hemosorption to these hospitals or by borrowing "artificial kidney" units from the other hospitals (whichever is more suitable). In order to eliminate hyperhydration in poisoning by hepato- and nephrotoxic poisons in the presence of toxic pulmonary edema, ultrafiltration of blood, also by means of an artificial kidney, is indicated. The complex of therapeutic measures conducted for poisoning is shown in Table 3. Of course, this table does not include all types of acute mass poisonings encountered in clinical practice. It presents only examples reflecting the general approach to organizing comprehensive therapy of mass poisonings.

Table 3. Basic Elements of Comprehensive Treatment of Acute Mass Poisonings

		Symptomatic Treatment of Disturbances of			Detoxication of the Body				
Type of Poisoning	Antidote and Specific Pathogenic Therapy	Hemodynamics	Respiration	Homeostasis	Forced Diuresis	Hemodialysis	Hemosorption	Hyperbaric Oxygenation	Blood Ultrafiltration
Gases with irritating, suffocating, burning action	Corticosteroids, antihistamine drugs	Treatment of shock	Inhalation, artificial respiration	Elimination of blood clotting and acidosis	-	-	-	-	With pronounced pulmonary hyperhydration
Methanol	Ethanol	Treatment of shock	Artificial respiration	Establishment of acidosis	+	+	-	-	-

Table 3. Basic Elements of Comprehensive Treatment of Acute Mass Poisonings (Continued)

		Symptomatic Treatment of Disturbances of			Detoxication of the Body				
Type of Poisoning	Antidote and Specific Pathogenic Therapy	Hemodynamics	Respiration	Homeostasis	Forced Diuresis	Hemodialysis	Hemosorption	Hyperbaric Oxygenation	Blood Ultrafiltration
Cellosolve	Ethanol	Treatment of shock	Artificial respiration	Establishment of acidosis	+	+	+	-	+
Carbon monoxide	Oxygen, cytochrome C, ascorbic acid, vitamin B_1	Treatment of shock	Artificial respiration	Establishment of acidosis	-	-	-	+	-
Mercury vapors	Unithiol, cuprenil	-	-	-	+	+	-	-	+
Chlorobenzene	-	-	-	-	+	-	-	-	-
Food poisoning (including by mushrooms)	Lipoic acid	Treatment of shock	-	Elimination of acidosis, blood clotting, coagulopathy	+	+	+	+	+

As victims recover, the need arises for expert assessment of ability to work, for rehabilitation, and for organization of dispensary observation. For patients surviving mass industrial poisoning, expert assessment of ability to work, plus rehabilitation, must be carried out cooperatively with the participation of an occupational pathologist and a representative of the trade union committee. Restoration of the ability to work must be assessed not only on the basis of signs of somatic recovery, but also on the basis of the victim's occupation and the possibility of his performing his duties. Patients must be rehabilitated in rehabilitation departments of toxicological centers or general treatment hospitals, with subsequent referral (when indications are appropriate) to sanatorium and health resort treatment. All victims surviving acute poisoning must be placed under dispensary observation. The frequency and length of observation depend on the severity of the poisoning, but patients must be examined at least once a year and must be kept under observation for at least one year.

References

1. Marshall, V., "Osnovnyye opasnosti khimicheskikh proizvodstv" [The Main Dangers of Chemical Production Operations], Moscow, 1989.

2. Mackenzie, D., NEW SCI., Vol 104 No 1433, 1984, p 9.

Prolonged Crush Syndrome. Communication II. Treatment, Complications, Outcomes

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[Article by G. N. Tsybulyak]

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[Text] Treatment of the prolonged crush syndrome (PCS) must be intensive from the very beginning, and it must include critical care measures aimed essentially at actively preventing complications. The general goals of the medical care for PCS may be stated briefly as follows: in the prehospital period—effective pain relief, the earliest possible alkalinization of the body (intravenously and perorally), and prevention of catastrophic plasma loss by means of tight bandaging (with an elastic bandage); in the hospital stage—emergency treatment of hyperkalemia and acidosis, active infusion therapy and prevention of acute renal insufficiency (ARI) and suppurative-infectious and septic complications; when ARI has already developed—hemosorption methods of cleaning out the body, or hookup of an "artificial kidney" unit; in the period of recovery—greater attention to general fortifying therapy and prevention of late complications, especially on the part of the kidneys (pyelonephritis).[13] Assessment of the viability of limbs and the earliest possible identification of necrotic changes in order to enable timely fasciotomy, necrectomy or amputation has a special place in all of the stages.[21,27] The organizational side of the effort is quite important, inasmuch as favorable results in the treatment of PCS on the level offered by today's medicine can be achieved only in specialized treatment facilities that provide the conditions for intensive care and programmed hemodialysis and hemosorption.[9] Constant monitoring of pH, the gas composition of blood, and the electrolyte level in blood and urine plays a great role in preventing possibly lethal disturbances in homeostasis.

When rendering first aid, pain relief would ideally be provided before pulling victims from beneath rubble and debris. Analgesics of the narcotic series and of other groups

(omnopon, promedol, analgin combined with dimedrol, etc.) are suitable for prehospital pain relief. When necessary (in the case of a mentally and emotionally excited patient), these analgesics may be combined with sibazon (seduxen, relanium) and other tranquilizers. Ketamine (ketalar, ketanest) is enjoying increasingly greater acceptance in prehospital pain relief for trauma; it is best combined with seduxen; doses that produce an analgesic effect are used—0.5-1 mg/kg IV or IM.[8] Exceeding the recommended doses causes what is an undesirable anesthetization by the time the victim is admitted to the hospital, inasmuch as it makes diagnosis extremely difficult as a result of loss of contact with the patient and distortion of the clinical pattern of cerebrocranial trauma and internal injuries. Blockades (affecting transmission) via the use of local anesthetics and inhalation of nitrous oxide with oxygen (through an anesthesia mask), trichlorethylene, or inhalan (through special Tringal or Analgizer vaporizers) may be performed in a special ambulance. For open injuries, it is advisable to add to novocaine (trimecaine) solution modern broad-spectrum antibiotics, which greatly improve the prospects for controlling infection. Immobilization of the entire injured limb is mandatory when injury to soft tissue is considerable, especially with bone fractures. It is advisable to use pneumatic splints, which promote prevention of plasma loss through moderate compression of the limb. Methods for cooling the injured limb increase in importance when a victim must undergo lengthy transport. Application of a tourniquet on an injured limb is not advisable in PCS: if tissues are still viable, the tourniquet will not prevent toxemia, and it will aggravate ischemia and intoxication of the body. Prolonged application of a tourniquet increases the risk of additional damage to nerves and vessels and promotes formation of ischemic contractures; application of a tourniquet for more than two hours leads to necrosis of the limb. The desire to use a tourniquet to block the outflow of toxins deposited in a necrotic segment had seemed logical before, right up until the moment of amputation. But the fact is that, as a rule, it is difficult to diagnose complete necrosis of a limb in the early stages of PCS; the moment most victims with PCS are freed from beneath rubble, their peripheral arteries are still pumping,[19] and the criteria for nonviability that are applied in ischemic necrosis of a limb (absence of all sensitivity, the impossibility of active and passive movements) are unreliable in PCS.[26,29,32,33] Of course, recommendations concerning the inadvisability of applying a tourniquet do not apply to cases of profuse hemorrhaging of wounds, total destruction, and massive crushing, in which the primary indications raise no doubts as to the need for amputation. In such cases the tourniquet is not removed until the limb is removed above the point of its application.

In the system of measures of prehospital care for PCS, special emphasis is placed today on early alkalinization of the body by intravenous injection of sodium hydrocarbonate, active infusion of crystalloids, and early administration of cyclics [petlevyye] and osmodiuretics (lasix, mannitol).[29,33] This promotes effective elimination of myoglobin from the body and prevents development of ARI and other complications, thus promoting preservation of both life and limb. Solutions containing potassium (Ringer's, Hartmann's, Lactasol) must be excluded from infusion therapy.

Control of hyperkalemia in the hospital stage requires immediate intravenous infusion of a hypertonic (40 percent) solution of glucose (50 ml) and insulin, and a 10 percent solution of calcium chloride or gluconate (30 ml in 20 min). Further systematic monitoring of the potassium level in plasma has the objective of promptly revealing and eliminating critical concentrations (7 milliequivalents per liter) in order to prevent hyperkalemic stoppage of the heart. If the plasma potassium level has exceeded 7 milliequivalents per liter, immediate use of adsorbents (polystyrene sulfonate) and hemo- or peritoneal dialysis are indicated, in addition to the glucose together with insulin and calcium preparations.[36] A catheter is inserted in one of the larger veins (superior vena cava, femoral) to enable direct, multiple infusions. Arterial and central venous pressure, diuresis and other parameters are systematically monitored. A permanent catheter is introduced into the urinary bladder during the time of forced diuresis in order to measure hourly urine elimination, the pH of urine, and the urine's qualitative composition (myoglobin, erythrocytes, protein, cylinders). The concentration of urea and electrolytes in blood should be determined every six hours.[26,29] Alkalinization of the body in the hospital is continued by means of systematic addition of 45.5 milliequivalents of sodium hydrocarbonate (4 percent solution—93 ml) to every 2 liters of infused liquid, in order to keep the pH of the urine at a level exceeding 6.5.[26,29,32,33] Indications for administering diuretics arise when diuresis is less than 300 ml/hr against the backdrop of active infusion of solutions.[29,32] When the pH of the urine is less than 6.5, administration of a carbonic anhydrase inhibitor—diacarb (acetazolamide, 250 mg), the diuretic effect of which is based on change of the acid-base balance in the body, is indicated.[26,29,32,33] A rate of infusion of 300-500 ml/hr is considered to be adequate in PCS, because it corrects hypovolemia rather quickly and stabilizes hemodynamics.[36] Another objective of infusion therapy is achieved at the same time—restoration of oncotic blood pressure through transfusion of blood plasma and of albumin and polyglucin solutions. Prescription of hemodex [gemodez] (neocompensan) and rheopolyglucin is indicated in the early stages (in the first hours) with the purpose of detoxifying the body. Because it possesses a high and stable buffer capacity, use of 0.3 M THAM buffer is recommended as a means of alkalinization in PCS.[12] If the victim's swallowing reflex is intact, sodium hydrocarbonate is prescribed per os (2-4 gm every 4 hr) over the next two to three days. When diuretics are administered, hypovolemia must be corrected by anticipatory active infusion of blood plasma and of albumin and crystalloid solutions.

Epidural analgesia (at level T_{11}-L_1) has proven to be effective as a means of pain relief in cases involving crushing of the lower limbs, the waist area and the pelvis. Fully controllable analgesia is thus achieved, mental status

improves, peripheral vasoconstriction is eliminated, arterial hypertension is corrected, and circulation in the kidneys and the injured limbs is improved.[18] A paranephral novocaine blockade is not very effective in PCS.[12] All authors correctly emphasize the need for starting intensive care as soon as possible in PCS, since the changes most typical of it take shape in the first five to six hours after injury.

When there is no response to stimulation of diuresis, neither lasix nor mannitol should be prescribed again, inasmuch as tubular necrosis has already developed in the kidneys. To save the lives of such patients, hemosorption and hemodialysis is urgently required. The need for early administration of hemodex [gemodez] and rheopolyglucin (detoxication of the body) and, on the 6th or 7th day after injury, thawed cryogenically preserved erythrocytes (to normalize the blood's coagulating properties) has been confirmed in experiments specially devoted to studying the effectiveness of infusion therapy in PCS.[3] It is recommended that stimulation of diuresis be begun by infusing 500 ml of 0.85 percent sodium chloride solution in 5 percent glucose solution. When there is no diuretic response to infusion (diuresis less than 300 ml/hr) and when central venous pressure concurrently rises above 5 cm H_2O, administration of 20 percent mannitol solution is indicated (at a rate of 1 gm/kg, intravenous stream); 44.5 milliequivalents of sodium hydrocarbonate (4 percent solution—93 ml) are added subsequently to each 500 ml of 0.85 percent sodium chloride solution in 5 percent glucose solution.[33] Based on the experience of treating victims of the Armenian earthquake, special emphasis is now placed on administering higher volumes of fresh-frozen plasma (1.5-2 liters), heparin (10,000-20,000 U) and 5 percent albumin. Blood transfusion was required in many cases; detoxication required the use of enterodex [enterodez], and activated charcoal per os; hemodialysis and endovasal laser therapy were conducted according to indications; immunocorrection was performed with hyperimmune plasma, gamma-globulin and lysozyme.[2]

The possibilities of infusion therapy alone are limited in PCS; sanitation of the injured limb, detoxication of the entire body and active protection of the kidneys are required concurrently. Disarticulation of a crushed limb in animal experiments prior to removal of the crushing load saved the lives of the animals against the backdrop of a 100 percent mortality rate in control.[11,12] By hooking up an "artificial kidney" (an X-100 dialysis machine) to the perfusion loop of the injured limb and carrying out ultrafiltration, myoglobin can be adsorbed and edema of the limb can be prevented.[17] Connection of a donor pig liver quickly normalizes metabolic disorders both in experiment and in the clinic; chunks of donor liver preserved in liquid nitrogen and retaining functional properties after defrosting are also effective.[11] However, the methods of connecting a donor liver, especially under the conditions of regional perfusion, are rather complex. They require live donor pigs and, most important, are not sufficiently effective, since after the donor liver is disconnected, uptake of toxic products still continues. For that reason, a large amount of attention is being devoted to simpler and more reliable detoxication techniques—hemo- and lymphosorption. Through repeated treatments, sorbents (SKN charcoals and others) reduce the concentration of potassium, phosphates and a number of toxins in blood. Potassium and acid metabolites are readily absorbed in regional hemosorption.[1] Variations of hemo- and lymphosorption in which blood and lymph draining from damaged segments are returned after sorption to vessels associated with the superior vena cava are effective.[17] Moderate and severe PCS are themselves an indication for hemosorption, while development of ARI is an indication for the beginning of hemodialysis.[15] An important conclusion was made concerning the treatment of victims with severe PCS: simultaneous hemosorption (with SKN, KAU, and other charcoals) and hemodialysis are necessary. Sorption makes it possible to successfully eliminate encephalopathy, and it improves overall condition, but it does little to change the level of urea and creatinine in blood. Hemodialysis effectively corrects hyperazotemia and hyperhydration.[20] Lymphodialysis combined with hemosorption and ultraviolet irradiation of blood were found to be effective in the early period of treatment of 112 patients with PCS. In the ARI stage, in the presence of the hypodynamic type of hemodynamic disturbance, hemosorption and lymphogenic methods of purification and ultraviolet irradiation are indicated; whereas in the hyperdynamic type, a combination of hemodialysis and hemosorption, the detoxifying effect of which is prolonged by lymphogenic purification methods, is indicated.[16] Hemodialysis must be early and regular, and it must be tailored to the individual, depending on the level of catabolism; life-threatening hyperkalemia and hyperhydration are absolute indications for hooking up an "artificial kidney."[24] Hyperbaric oxygenation in combined PCS therapy enables faster elimination of blood hypoxia, increase of thrombocyte concentration, reduction of intoxication, and improvement of kidney function.[10] However, not all researchers confirm that hyperbaric oxygenation has a favorable effect in prolonged tissue crushing.[36] The experience of early and extensive plasmapheresis in combined PCS therapy indicates that the therapy is highly effective in eliminating the disseminated intravascular clotting syndrome, in detoxifying the body, and in preventing ARI; this makes it possible to go directly from the oliguria stage to the polyuria stage, bypassing the most dangerous anuria stage.[6]

The most important aspect of PCS therapy is that it resolve the fate of the injured limb (fasciotomy, necrectomy, amputation). A completely unviable limb or its segment needs to be amputated immediately. Amputation of a viable limb that has become the cause of ARI is contraindicated, inasmuch as such an operation would not avert the manifestations of the syndrome, but would sharply worsen the condition of the victims. However, in major handbooks of recent years, one can still find the recommendation for early amputation if edema of the injured limb is very pronounced and if all forms of sensitivity and active and passive movements are absent, notwithstanding continuing pulsation of peripheral arteries.[36] The necessity

of amputation is sometimes dictated by developing secondary complications such as sepsis or infected gangrene. As was mentioned earlier, necrosis of a limb is determined not by the length of time of crushing, but chiefly by the nature of the anatomical injuries in PCS, which is why the call to amputate a limb on site without freeing it after 15 hours or more of crushing cannot be considered justified.[14]

Another actively debated question of surgical treatment of PCS concerns fasciotomy. Most researchers—both in the past and in recent years—feel that it is urgently necessary to subject muscles to perform emergency decompression in the presence of increasing edema and weakening peripheral pulsation.[13,28] Sizable volumes of fluid that leave the vascular channel as a result of ischemic injury to the vascular endothelium cause a 30-60 percent increase in muscle volume, and this alone poses a real threat of necrosis to the segment or the entire limb.[35] However, fasciotomy carries the threat of massive exudation, wound emaciation and sepsis, which promote an unfavorable outcome in PCS, and hemorrhaging of surgical wounds can, to some extent, be an obstacle to the hook-up of an "artificial kidney" (heparinization is required). On this basis, some authors reject the advisability of fasciotomy altogether,[9,19] while others believe that it is indicated in the treatment of moderately severe forms of PCS.[4] We cannot agree with the arguments against fasciotomy that are based on the notion that nephrologists are able to do without it, inasmuch as they are focused on treatment of ARI, while surgeons, who are concerned chiefly with local treatment, lose patients much more often.[4] Complete rejection of the indications for fasciotomy should be seen as a mistake, but it is just as impermissible to widen the indications for this complex, critical operation. Determining objective criteria for excising fascias within the zone of a damaged segment is an important area of study. Most such criteria are based on measuring pressure in the subfascial space by means of needles, cannulas, catheters and wick-type drains.[25,31] If the measured value of subfascial pressure exceeds 30 mm Hg, immediate decompression of muscles (extensive excision of fascias) in all osseofascial sheathes is indicated.[36] Neurological disorders accompanying PCS cannot serve as an indication for fasciotomy. The experience of treating 103 victims suffering acute posttraumatic strangulation of muscles against the backdrop of massive edema led to the conclusion that early decompression of such muscles is required.[30]

In the opinion of surgeons who provided aid to victims of the earthquake in Armenia, subcutaneous fasciotomy is not justified.[15] Secondary sutures must be applied to wounds 7-10 days after edema drops off. Radical surgical treatment of the focus of injury, coupled with necessary removal of all unviable tissues, is often required in the course of fasciotomy. Sometimes the need for amputating the limb or a segment becomes obvious in the course of exploration, and it must be undertaken without delay or vacillation (in the presence of extensive or total necrosis of muscles, severe destruction, ruptures or scalping). Bone fractures discovered in the course of exploration should be stabilized in the final stage of the operation; methods of extrafocal fixation of fractures are preferred. It is recommended that the wound surfaces that are formed be covered with a screen of artificial material[21] or with a dressing covered with water-soluble ointment (levosin),[25] or that they heal in a controllable abacterial environment.[22] When an ordinary wet dressing that dries out with time is used, it must be changed regularly, at least twice a day. The principle of active wound healing presupposes early dermal and osteoplastic operations. Keeping the limb horizontal is recommended in the postoperative period, since arterial inflow is hindered and metabolic disorders of ischemic nature are aggravated when it is in an elevated position.[23] In recent years specialists who have provided aid to victims of aerial bombardment and artillery shelling have narrowed the indications for fasciotomy and other surgical procedures in the treatment of PCS to a minimum; however, even they adhere unfailingly to the rule of removing all necrotic tissues, which serve as a morphological substrate of intoxication, ARI and septic infection, often leading to lethal outcomes.[26,29,32,33] Maximally complete and early removal of unviable tissues from wounds, crushed areas and regions of ischemic necrosis, which are an ideal medium for multiplication of microbes, also remains primary to infection control. No antibiotics will be effective until necrotic tissue is removed. Microbial contamination does, in fact, occur later with closed injuries than with wounds and operations, which create the preconditions for faster development of septicopyemic complications. Infection in PCS tends toward metastasis and formation of secondary suppurative foci in internal organs. *Staphylococcus*, *Pseudomonas*, and fungi are identified relatively more often in bacteriological analysis of material from foci of suppurative infection; *E. coli* is isolated from blood; *Pseudomonas* is often the cause of septic shock.[29] Nonclostridial anaerobes were detected within the composition of wound microflora in 15 percent of the cases among victims of the Armenian earthquake.[15] In light of the marked weakening of anti-infection barriers in PCS, a catheter must not be kept in the same vessel for a period of any length (over 48 hours), and when sepsis is suspected, prolonged catheterization is altogether impermissible.[36] Highly active antibiotics devoid of nephrotoxic properties must be administered systematically from the first stages of treatment. Treatment is initiated with prescription of the sodium salt of penicillin at 5 million units every four hours with 0.85 percent sodium chloride solution administered over a period of 20 minutes, plus ampicillin at a dose of 0.5 gm twice a day. Treatment is changed to administration of cephalosporins after five days.

Administration of adrenocortical hormones is acknowledged to be advisable in PCS. Having a pronounced effect on metabolism, they promote favorable restructuring of the body under extreme conditions. Participation of cortisone in regulation of cellular lysosomes in the liver in PCS has been experimentally confirmed[11]; the effectiveness of protease inhibitors—Trasylol, kontrikal, ingitril—has been shown.[23] The immunostimulatory drugs timalin and timogen promote improvement of overall condition and

wound healing.[15] Administration of prostenon (prostaglandin E_2) is suggested for effective treatment of ARI, including in PCS; protection of the kidneys is so effective in this case that in many instances hemodialysis can be dispensed with.[7] In the late period of PCS, the main attention should be focused on treating local disorders—wounds, contractures, limited mobility in joints, traumatic nephritis (physiotherapeutic methods).

The mortality rate associated with PCS was 70 percent during World War II, while in peacetime it does not exceed 26 percent.[36] Victims may die in the acute period, before recovering from shock (5 percent), or later on, as a result of ARI (85 percent) and pulmonary complications (10 percent).[13] Gastric hemorrhaging resulting from necrosis of the mucous membrane (the disseminated intravascular clotting syndrome) is the cause of death more rarely.[5,34] Kidney function is restored 5-33 days after injury.[29] In cases that do not end in death, severe disability develops very often (in 70 percent of the cases), resulting from amputation of a limb, atrophy of muscles, contractures, and nerve paralysis.

References

1. Afanasyev, V. A. and Kreynes, V. M., in ""Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey" [Targeted Treatment of Severe Traumatic Ischemia of the Limbs], Kemerovo, 1978, pp 44-48.

2. Bazanova, E. B., Arzhakova, N. I. and Kayumov, Yu. Kh., in "Aktualnyye voprosy meditsinskogo obespecheniya porazhennykh na etapakh meditsinskoy evakuatsii" [Urgent Problems of Medical Support for Casualties at Stages of Medical Evacuation], Kazan, 1989, pp 43-44.

3. Beridze, A. A., "Experimental Justification of Transfusion Therapy for Prolonged Crush Syndrome," Doctoral Dissertation in Pursuit of the Academic Degree of Candidate of Medical Sciences, Tbilisi, 1982.

4. Borodulin, S. N., "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 68-71.

5. Vitter, V. I. and Ostanin, V. Ya., in "Klinicheskiye aspekty travmatologii i ortopedii" [Clinical Aspects of Traumatology and Orthopedics], Izhevsk, 1979, pp 167-169.

6. Vorobyev, V. P., Andreyev, Yu. N. and Gorodetskiy, V. M, "Aktualnyye voprosy meditsinskogo obespecheniya porazhennykh na etapakh meditsinskoy evakuatsii," Kazan, 1989, pp 7-9.

7. Glants, R. M., Kachorovskiy, B. V., Turchin, V. L. et al., "Aktualnyye voprosy meditsinskogo obespecheniya porazhennykh na etapakh meditsinskoy evakuatsii," Kazan, 1989, pp 12-14.

8. Danilevich, Ye. Ya., "Ketamine Anesthesia in Casualties With Severe Trauma and Shock, and Provision of First Aid," Doctoral Dissertation in Pursuit of the Academic Degree of Candidate of Medical Sciences, Leningrad, 1988.

9. Zakharova, G. N., Fursayev, V. A. and Polozov, A. B., VESTN. KHIR., No 2, 1978, pp 109-113.

10. Krivulis, D. B., Groshev, A. N., Tsimermans, G. I. et al., in "Giperbaricheskaya oksigenatsiya" [Hyperbaric Oxygenation], Moscow, 1985, pp 39-40.

11. Krichevskiy, A. L., "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 29-31.

12. Kuzin, M. I., in "BME" [Great Medical Encyclopedia], 3d Edition, Moscow, Vol 25, 1985, pp 188-190.

13. Kuzin, M. I., Sorokina, M. I., Troynyakov, N. K. et al., in "Osnovopolozhniki sovetskoy voyenno-polevoy khirurgii" [Founders of Soviet Military Field Surgery], Moscow, 1976, pp 31-33.

14. Mullin, I. A., "Aktualnyye voprosy meditsinskogo obespecheniya porazhennykh na etapakh meditsinskoy evakuatsii," Kazan, 1989, pp 74-75.

15. Nechayev, E. L., Lizanets, M. I., Bryusov, P. G. et al., VOYEN.-MED. ZHURN., No 4, 1989, pp 11-14.

16. Novikova, R. I., Shano, V. P., Logvinenko, L. V. et al., "Aktualnyye voprosy meditsinskogo obespecheniya porazhennykh na etapakh meditsinskoy evakuatsii," Kazan, 1989, pp 43-44.

17. Plotnikov, P. A., "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 41-44.

18. Savushkin, N. V., Mikheyev, V. I. and Zakharov, B. R., in "Sovremennyye problemy anesteziologii, reanimatologii, intensivnoy terapii" [Modern Problems of Anesthesiology, Resuscitation and Intensive Care], Alma-Ata, 1984, pp 291-293.

19. Sernyak, P. S., Kovalenko, N. V., Logvinenko, L. V. et al., VOYEN.-MED. ZHURN., No 5, 1978, pp 28-32.

20. Stanislavskiy, O. K., in "Spetsializirovannaya meditsinskaya pomoshch" [Specialized Medical Aid], Moscow, 1982, pp 144-145.

21. Torbenko, V. P., Popova, M. M., Rodin, B. M. et al., "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 37-41.

22. Fedorov, V. D., Kostyuchenok, B. M., Amirsalanov, Yu. A. et al., "Aktualnyye voprosy meditsinskogo obespecheniya porazhennykh na etapakh meditsinskoy evakuatsii," Kazan, 1989, pp 99-100.

23. Kharchenko, V. V., Protsenko, V. A. et al., FARMAKOLOGIYA, Vol 40 No 2, 1977, pp 187-190.

24. Shrayer, G. I., Krichevskiy, A. L. and Osipov, L. Ye. "Napravlennoye lecheniye tyazheloy travmaticheskoy ishemii konechnostey," Kemerovo, 1978, pp 76-79.

25. Becker, H., Gerngrob, H. et al., UNFALLCHIRURGIE, Vol 90 No 5, 1987, pp 212-217.

26. Bursztein, S., in "Annual Symposium on Critical Care Medicine, 23rd: Proceedings," Las Vegas, 1985, pp 497-499.

27. Kelly, R. and Whitesides, T., J. BONE JT. SURG., Vol 49-A, 1967, pp 1022-1027.

28. Martin, D., Z. ARZTL. FORTBILD., Vol 74 No 4, 1980, pp 168-169.

29. Michaelson, M., Taitelman, V. and Bursztein, S., RESUSCITATION, Vol 12 No 2, 1984, pp 141-146.

30. Oestern, H. and Echtermeyer, V., LANGENBECKS ARCH. CHIR., Vol 358, 1982, pp 227-232.

31. Owen, C., Mubarak, S. et al., NEW ENGL. J. MED., Vol 300 No 21, 1979, pp 1169-1172.

32. Reis, N. and Michaelson, M., J. BONE JT. SURG., Vol 68-A No 3, 1986, pp 414-418.

33. Ron, D., Taitelman, U. et al., ARCH. INTERN. MED., Vol 144 No 2, 1984, pp 277-289.

34. Santangelo, M., Usberti, M. et al., SURG. GYNEC. OBSTET., Vol 154 No 5, 1982, pp 372-374.

35. Schmit-Neverburg, K., LANGENBECKS ARCH. CHIR., Vol 358, 1982, pp 221-226.

36. Wiener, S. and Barrett, J., in "Trauma Management for Civilian and Military Physicians," Philadelphia, 1986, pp 23-26.

Comprehensive Detoxication in Acute Renal Insufficiency in Patients With Prolonged Compression Syndrome

917C0304F Moscow TERAPEVTICHESKIY ARKHIV in Russian Vol 62 No 10, Oct 90 (manuscript received 20 Feb 90) pp 21-25

[Article by I. I. Shimanko, Scientific Research Institute of First Aid imeni N. V. Sklifosovskiy, Moscow]

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[Text] The prolonged compression syndrome (PCoS), or crush syndrome, was first described by Bywaters and Beall, who had observed compression of the limbs of people by fragments of destroyed buildings during aerial bombardment of Great Britain in 1941. Such injuries were observed in the Great Patriotic War, during the war in Vietnam, and in the earthquakes in Ashkhabad and especially in Armenia. Severe mechanical injury coupled with pronounced endotoxemia leading to the development of acute renal insufficiency (ARI) is encountered rather often in medical practice in various injuries: (1) with isolated PCoS and a routine variety of it—the syndrome of static compression of soft tissues by the weight of the body of a comatose patient; (2) with PCoS combined with trauma (extensive injury to soft tissues); (3) with PCoS coupled with bone damage; (4) with PCoS complicated by a suppurative-septic condition and trauma to major vessels; (5) with PCoS complicated by acute hepatorenal insufficiency (AHRI).

One of the principal causes of a severe course of PCoS and lethal outcomes is entry of toxic substances (myoglobin, inorganic phosphorus, potassium, creatinine, histamine-like substances, medium and high molecular weight peptides, incompletely oxidized toxic metabolites) from injured tissues into the body with the flow of blood and lymph. When assessing the severity of the state of victims, we must take into consideration the length of crushing time and force, the extent of the area of injury, and the probability of complications on the part of other organs. Severe mechanical trauma involving the crushing of soft tissues is always accompanied by disturbance of the principal indicators of homeostasis and by pronounced endotoxicosis.

Specific notions have developed concerning the comprehensive mechanism of the development of ARI in PCoS (or the crushing of muscle fibrils). The causes of development of ARI are as follows: (1) neuroreflexive and neurohumoral factors caused by lengthy painful stimulation; (2) pronounced plasma loss; (3) toxemia. Endotoxicosis is one of the leading pathogenic components of the development of ARI in patients with severe compression trauma. Soft tissues and, in particular, striated muscles that are rendered ischemic by compression serve as the source of this toxicosis. Toxic substances are found to have a pronounced vasoconstrictive action upon glomerular vessels, and they affect the epithelia of renal canaliculi, thereby impairing renal function considerably and promoting development of ARI.

Thus several etiopathogenic factors are responsible for the appearance of ARI in PCoS, or the syndrome involving the crushing of myofibrils. They include crushing or compression of soft tissues, decompression, and traumatic shock. PCoS manifests itself as pain and tourniquet shock after decompression, as a result of which pronounced hemodynamic disturbances arise (collapse, disturbance of central hemodynamics). Local changes are typified by pronounced tissue destruction accompanied by mechanical disintegration of lysosomes. Edema of the limb, coupled with growing plasma loss, which results in thickening of the blood, develops after decompression. Morphological trauma to muscles manifests itself as their aseptic coagulational necrosis, and in myoglobin transport (myoglobinemia and myoglobinurea), as pigment nephrosis (shock kidney).

Thus, the myorenal syndrome leads to ARI, manifesting itself as sharply pronounced disturbance of homeostasis. Hyperazotemia, hypercreatininemia, anemia, tissue hypoxia and pronounced metabolic acidosis are revealed by laboratory tests. ARI in skin damage associated with crushing is often accompanied by severe suppurative-septic complications. In its acute period, PCoS is accompanied by hepatopathy against the backdrop of pain and tourniquet shock. Compression of soft tissues of the limbs elicits a slowdown of hepatic circulation and dystrophic changes in hepatic cells, coupled with depletion of protein and carbohydrate reserves in the liver. Circulatory decompensation in the limbs is accompanied by the addition of

thrombosis of hepatic vessels, necrobiosis of liver cells, edema of hepatic parenchyma and growth of toxicity of blood serum.

Disturbance of hemodynamics, respiratory suppression, skin pallor, cold sweats, general weakness, thirst, sluggishness, sleepiness and headaches are revealed in pronounced endotoxemia; disturbance of kidney function is found with oligonuria. Sharp restriction or absence of movement in joints, reduction or absence of pain and tactile sensitivity, paresis and pain in the injured area are also observed.

Local changes in crushed tissues manifest themselves as considerable edema of the injured area, intermuscular and subcutaneous hematomas and excoriations; extensive crushing and contused-lacerated wounds are present as well. When the area of crushed soft tissues is large, trauma to nerves and damage to arteries, accompanied by massive hemorrhaging, are especially dangerous. In these cases the limb is cold to the touch and exhibits a "woody" induration and the skin is imbibed with blood and bears a marbled pattern, often combined with sloughing of epidermis and formation of phlyctenae.

When AHRI develops, disturbance of the water balance manifests itself primarily as hyperhydration: extracellular, intracellular and general. As a rule, disturbance of water volumes, of electrolyte content, and of osmolality in one sector—in the intracellular sector, for example—leads to corresponding intracellular disorders. As a result of disturbance of water metabolism taking the form of intracellular hyperhydration coupled with water retention, first in the vascular channel and then in the interstitia, hyperkinetic impairment of circulation occurs. As AHRI proceeds and the water balance is disturbed further, fluid shifts into the intracellular sector, and general hyperhydration coupled with hypokinetic circulation develops.

Myoglobinemia from 400 to 100,000 ng/ml and myoglobinuria from 200 to 800 ng/ml are observed in all patients with crushed soft tissues upon admission to the hospital. The level of myoglobinemia depends on the area and force of compression of soft tissues. The content of midweight molecules exceeds the norm by 40-70 percent. Hyperazotemia, hypercreatininemia, hyperenzymemia and moderately expressed bilirubinemia are determined in all cases. The impaired respiration syndrome is observed in patients with second- and third-degree nephrohepatopathy, and it is accompanied by worsening of pulmonary ventilation, coupled with a decline in oxygen tension in arterial blood to 30-45 mm Hg. The principal cause of respiratory disorders is second- and third-degree pulmonary hyperhydration against the backdrop of a negative water balance. Hyperhydration develops in patients as a result of excessive intake of fluids into the body through drinking or intravenous administration. Metabolic acidosis is noted in all patients with respiratory disorders.

Analysis of medical care rendered to patients with PCoS has revealed extremely serious shortcomings in that care in the early, prehospital stage, w[illegible] subsequently severely complicates the implementation of therapeutic measures and sometimes leads to a lethal outcome. For example, in the absence of sufficient and objective criteria for assessing viability of compressed limbs, especially in the early period of PCoS, and without allowances made for further growth of edema of limbs, which makes it difficult to determine the extent and depth of zones of aseptic coagulational necrosis and, consequently, the level of amputation, amputations have been carried out unjustifiably early, with tight suturing of the stump, which has frequently required reamputation later on. Amputation is indicated only in cases of unquestionable unviability of tissues, severe traumatic shock and hemorrhaging—that is, when limbs are compressed by heavy beams and large loads with obvious crushing and kneading of tissues and with bone fractures.

Trouser-stripe [lampasnyye] incisions, what are called trouser-stripe incisions—that is, numerous incisions of the skin that damage nerves—are, in our opinion, absolutely contraindicated, as with fasciotomy, since disturbance of the integrity of the skin leads to suppurative-septic complications, going as far as development of tetanus and gas infection. This is accompanied by the most diverse complications in the early period and especially in the remote period and substantially hinders adequate dialysis and filtration therapy. Subsequently, in a later period, when there is infection and intensive absorption of toxins accompanied by plasma loss and reduction of edema, massive hemorrhaging from eroded vessels recurs in the area of infection and necrosis. Generalized sepsis develops in some patients. When they heal, trouser-stripe incisions often produce deforming keloidal scars, which considerably lengthen the time of recovery of the function of injured limbs, the time needed for rehabilitation of patients and their release from the hospital, and recovery of performance.

When the integrity of skin cover is maintained in patients with pronounced edema of the limbs, repeated application of dialysis and filtration methods makes it possible to relieve edema very quickly and ensure early restoration of limb function and the patient's performance. When these methods are used, no complications of any sort arise, and they provide a possibility for ensuring faster restoration of kidney function.

Conservative therapy in the period of pronounced oliguria or anuria includes diet—menu No 7 with limited intake of salt and protein. Patients in a state of anuria or pronounced oliguria undergoing daily active detoxication are mandatorily subjected to daily infusion therapy to correct homeostasis. Its volume varies from 1,500 to 2,500 ml, depending on the fluid deficit created as a result of many hours of hemodialysis and filtration, arising in the course of removal of the toxic ultrafiltrate. The therapy includes prevention and treatment of cardiovascular and pulmonary disorders. Administration of sodium thiosulfate, which has a direct antidote action against "ischemic toxin," is indicated in the acute period of PCoS. Simultaneous intravenous administration of sodium thiosulfate in the early period of tourniquet shock helps to eliminate myocardial hypodynamia, improve the heart's contractile function, restore conduction and normalize peripheral vascular resistance.

Patency of the upper respiratory tract is restored when so indicated (by intubation, oxygenation). Antibiotic therapy is prescribed in the presence of pulmonary complications. Semisynthetic nontoxic antibiotics are used based on the presence of anuria and daily use of active dialysis and filtration methods.

Liver-protective therapy is prescribed in order to prevent and treat functional disorders of the liver: vitamins B_6, B_{12} and C, essentsiale, liv-52, 10 percent glucose solution, kontrikal (30,000 units per 100 ml of physiological solution), Trasylol or Gordox; glucose-novocaine mixture and rheopolyglucin are injected intravenously as well.

Water-electrolyte disturbances and acid-base balance are adjusted strictly according to laboratory indications: on the basis of the concentration of potassium, sodium, calcium and chlorides in blood plasma; if present, acidosis is carefully adjusted as a rule (with lactosol), trisamine, 4 percent or 8 percent sodium hydrocarbonate solution). Antiaggregants—Trental, Curantyl—are prescribed in hypercoagulation, while fibrinolytically active plasma is prescribed for the most pronounced hypercoagulation.

Transfusion of fresh-frozen plasma, washed erythrocytes, freshly obtained blood, albumin and protein is indicated in hemorrhages accompanied by plasma loss.

Prevention of infectious complications (antibiotics and antiseptics—dioksidin, metradzhil [transliteration]) and of immune deficiency is carried out with allowances made for ARI and AHRI—that is, use of hepato- and nephrotoxic compounds is excluded. Antistaphylococcal plasma, leukocyte mass, bacteriophages, taktivin and B-activin are additionally prescribed. Conservative detoxication therapy in oliguria or in early restoration of diuresis (over 250-300 ml of urine eliminated per day) includes stimulating diuresis (with lasix and furosemide intravenously); neohemodex [neogemodez] is administered, and intestinal sorption is conducted with charcoal sorbent and enterodex [enterodez].

The method of active therapy in the early period of ARI is chosen depending on arterial pressure; the content of urea, creatinine, electrolytes, hemoglobin, bilirubin and hepatic enzymes in blood; the hematocrit; the degree of oliguria; and the level of toxicity of blood and urine. In lymph drainage, it is selected depending on the content of midweight molecules in lymph and the myoglobin level in blood and urine. The degree of hydration of the lungs is determined radiologically. Use of active methods for various sectors and media of the body—blood, lymph, intestine—is a general principle of detoxication and correction of disturbed homeostasis. Conservative and surgical methods of detoxifying the body are prescribed for patients as a function of the markedness of endotoxemia and the degree of disturbance of liver and kidney functions. In the early period of toxemia, when diuresis is intact, conservative methods of detoxication are used, to include hemodilution, adjustment of acid-base balance and water-electrolyte metabolism, and forced diuresis. In the initial stage of infusion therapy, to normalize volemia and restore central hemodynamics, colloidal solutions with hemodynamic action (polyglucin, gelatinol, hemodex [gemodez] or neohemodex [neogemodez]), electrolyte solutions, and glucose solutions containing insulin are administered, and transfusions of blood and protein solutions are carried out.

Hemodilution is carried out by infusion of a 10 percent solution of albumin (3 ml/kg), protein (5-6 ml/kg), rheopolyglucin or neohemodex [neogemodez] (6-8 ml/kg), and solutions of crystalloids and glucose (10-15 ml/kg), to which disaggregants are added in order to improve microcirculation at the same time by reducing peripheral vascular resistance (heparin, Curantyl, Trental). Forced diuresis is conducted the moment the patient is admitted to the hospital against a backdrop of hemodilution in order to detoxify and free the blood of myoglobin and midweight molecules circulating within it. Diuresis is stimulated with 10 percent and 20 percent solutions of glucose and lasix (up to 200-300 mg/day). Patients are given 2,000-2,500 ml of various solutions daily (5 percent glucose solution, electrolyte solutions, isotonic sodium chloride solution). The quantity of solutions administered intravenously and per os is strictly monitored in terms of diuresis, loss of fluids through vomiting, diarrhea and perspiration, and hydration indicators (the lungs are subjected to radiography, and the OTsK, TsVD [not further expanded] and the hematocrit are determined). Artificial hemodilution and forced diuresis conducted on patients with endotoxemia in severe mechanical trauma involving the crushing of soft tissues are accompanied by a pronounced detoxifying effect manifesting itself as reduction of the content of myoglobin in blood as a result of its elimination with urine, and as a decrease in the level of toxicity of blood and the content of midweight molecules in it.

Sorption is one of the active methods of detoxication based on removing toxic substances and metabolites from the body's fluid media. Enterosorption includes dosed administration of sorbent per os, at a dosage of one tablespoon three or four times a day. It should be noted that the merit of enterosorption as a method of detoxication therapy is that it enables, on the one hand, selective control of mass exchange of toxic substances and the most important metabolites of the digestive juices of the gastrointestinal tract and blood and, on the other, blockade of the natural channel of transport of toxic compounds by menas of their absorption from intestinal contents, their elimination from blood, and prevention of reflux of endotoxins into blood.

Enterodex [enterodez], enterosorb and various types of charcoal are among the most active enterosorption agents used in endotoxicosis. When intestinal function is intact, their use artificially intensifies elimination of low and medium molecular weight substances from circulating blood, which promotes neutralization and reduction of toxin absorption from the gastrointestinal tract. The greatest detoxifying effect is achieved with the combined use of enterodex per os and neohemodex [neogemodex] intravenously. Improvement of the general condition of patients, normalization of sleep and appetite, disappearance of sensations of discomfort in the abdomen, and

improvement of intestinal function are noted in the clinical picture. At the same time, reduction of the levels of midweight molecules by 20-25% and of bilirubin by 20% in blood, and the concentrations of AST by 30%, ALT by 15% and LAD by 25% are observed. The sufficiently high therapeutic efficacy of the drugs, the simplicity of their use, and the absence of side effects enable the use of this method both in the prehospital stage of treatment and at hospitals.

Hyperbaric oxygenation, which improves microcirculation in organs and tissues as well as central and organ hemodynamics, is an effective means of fighting local and general hypoxia in endotoxicosis. Underlying the therapeutic effect of hyperbaric oxygenation is the substantial increase in the oxygen capacity of the body's fluid media, which makes it possible to quickly raise the concentration of oxygen in cells suffering from hypoxia as a result of severe endotoxicosis. Hyperbaric oxygenation in patients with acute ischemia and necrosis of the limbs as a result of mechanical trauma of soft tissues makes it possible to reduce edema in the injured area, improve overall condition and appetite, and normalize sleep. When extensive necrosis of crushed muscles and their suppuration are present, hyperbaric oxygenation treatments raise the level of the humoral factors of nonspecific defense and stimulate an increase in the quantity of T- and B-lymphocytes; the content of immunoglobulins rises considerably in this case. Use of hyperbaric oxygenation in traumatic endotoxicosis intensifies catabolic processes and slows down anabolic ones, and necrotic areas of muscles are quickly separated from healthy ones.

However, when PCoS is complicated by ARI, the primary principle of treatment is daily use of various active surgical methods of detoxication and correction of disturbed homeostasis for anuria. The choice of method (hemosorption, lymphosorption, dialysis and filtration, plasmapheresis) is determined daily as a function of the content of urea, creatinine, bilirubin, liver enzymes, hemoglobin and electrolytes in blood and lymph, as well as on the basis of the degree of oliguria or presence of anuria. The main indications for the use of surgical methods of detoxication are myoglobinemia and a high degree of toxicity of blood, lymph and urine, as determined from an elevated content of midweight molecules (above 0.800 conventional units), the paramecium test index (a life span of paramecia up to 7 min), a lymphocytic index of intoxication of 7.5, plasma potassium elevated to 8 millimoles per liter, an increase in blood urea to 27.6 nanomoles per liter and of creatinine to 232 nanomoles per liter, dramatic elevation of blood enzymes (ALT, AST, LDG, cholinesterase, alkaline phosphatase, aldolase), metabolic or mixed acidosis, and anuria.

Comprehensive therapy conducted on patients with crushed soft tissues includes anterograde catheterization of subcutaneous lymph collectors in the foot, calf or forearm. Endolymphatic therapy creates an optimum concentration of drug in the lymphatic system in "pure form" and ensures maximum contact of the drug with pathogenic microorganisms at the sites of their detention and accumulation, predominantly in lymph nodes. Prolonged endolymphatic administration of antiseptics, antibiotics, disaggregants, neohemodex [neogemodez] and rheopolyglucin in the course of comprehensive lymphatic drainage improves microcirculation and ensures the sanitation of traumatized soft tissues.

After endolymphatic therapy and prolonged or fractional intra-arterial infusion of drugs together with ultraviolet irradiation of blood and with hyperbaric oxygenation, the overall condition of patients improves; pain, edema and hyperemia decrease; separation of necrotic tissues and wound healing accelerate; the rheological properties of blood return to normal; formation of toxic metabolites decreases; and the elimination of metabolites from the body by way of the kidneys accelerates.

Use of active methods of cleansing various media and systems in the body—blood, lymph, intestine—is a general principle of detoxication and correction of disturbed homeostasis. Experience in treating patients with ARI, and especially with AHRI, has confirmed that it is extremely difficult to save PCoS patients with just one method for detoxication and correction of homeostasis. An individual approach is needed for selecting the complex of methods that is based on location of the compressed area, combination of injuries, hemorrhaging, level of toxicosis, and suppurative-septic complications. Simultaneous or successive application of the methods is required, and their optimum duration and the indications for each of them must be determined.

The indications for hemodialysis include uremic intoxication, anuria without pronounced hyperhydration, hyperkalemia, hypo- or hypernatremia, and disturbance of the acid-base balance that does not respond to infusion therapy. The contraindications for hemodialysis include arterial hypotension and acute hepatic insufficiency. However, because patients with PCoS exhibit anuria and pronounced hyperhydration in the acute period, the leading methods of detoxication, especially when toxic metabolites are present in blood and lymph, are filtration methods employing highly porous membranes that are highly permeable to fluids. For example, ultrafiltration is conducted with a highly permeable dialyzer and motor for 1-1.5 hours (without dialyzing solution). It may be carried out in rayon hospitals if patients cannot be transported. Marked hyperhydration is an indication for ultrafiltration as a vitally important resuscitation measure.

The indications for hemofiltration are as follows: uremic intoxication, unstable hemodynamics (arterial hyper- and hypotension), and hyperhydration of the lungs. Presence of acute hepatic insufficiency is not a contraindication for hemofiltration. A therapeutic effect is attained as a result of correction of central and organ hemodynamics, as well as of homeostasis through substitution of ultrafiltrate by electrolyte solutions, glucose and plasma-substituting solutions.

Simultaneous hemodialysis and filtration, in which the advantages of both methods are combined, is the most effective and up-to-date method of detoxication and correction of homeostasis. The therapeutic effect comes from

correction of the water-electrolyte balance and the acid-base balance and the normalization of gas exchange, the aggregate blood state system, central and peripheral hemodynamics and biochemical indicators. Clearance in relation to urea, creatinine, midweight molecules, bilirubin and myoglobin exceeds considerably clearance attained with hemodialysis and hemofiltration separately. With 5 to 6 hours of combined hemodialysis and filtration, clearance is 165 ml/min in relation to urea and 170 ml/min in relation to creatinine.

The experience of treating over 600 patients with PCoS complicated by ARI shows that use of the methods of comprehensive conservative and active therapy makes it possible to restore disturbed functions of the kidneys, liver and compressed limbs in most patients.

Effects of Low Intensity Ultrasound and ds-RNA on Lipid Peroxidation in Wound Healing

917C0500E Yerevan EKSPERIMENTALNAYA I KLINICHESKAYA MEDITSINA in Russian Vol 30 No 5, Sep-Oct 90 (manuscript received 20 Feb 90) pp 490-492

[Article by L. M. Ovsepyan, K. G. Karagezyan, S. S. Ovakimayn, S. M. Galstyan, A. A. Barsegyan, N. R. Margaryan, R. A. Zakharyan and Zh. I. Akopyan, Institute of Experimental Biology, Armenian SSR Academy of Sciences; Chair of Surgery, PSS f-tov [expansion unknown], Yerevan Medical Institute]

UDC 615.837.3+616-001.4

[Abstract] An analysis was conducted on the effect on lipid peroxidation in healing a skin wound of low-intensity ultrasonication (26.5 kHz, 35-40 μ amplitude oscillation, 3 min), using a Ca-dsRNA solution for energy transduction. Comparison of the level of lipid peroxidation in suture-closed wounds over six days in control and experimental outbred male rats (180-200 g) showed that the level of peroxides in the experimental group was 22.83 nmoles/g of tissue, and in the untreated rats 37.06 nmoles/g. Ultrasonication in combination with physiological saline rather than Ca-dsRNA yielded intermediate values of 32.43 nmoles/g. The potentiating action of dsRNA was attributed to activation of endogenous antioxidants. Tables 1; references 8: 6 Russian, 2 Western.

Wound Management With Immobilized Trypsin in Animals With Subacute Radiation Injuries

917C0500F Yerevan EKSPERIMENTALNAYA I KLINICHESKAYA MEDITSINA in Russian Vol 30 No 5, Sep-Oct 90 (manuscript received 13 Apr 87) pp 496-499

[Article by V. I. Pronin, L. Z. Velsher, G. N. Berchenko, M. P. Zverev, Ya. D. Kan, B. N. Arutyunyan and V. V. Ryltsev, Moscow Medical Stomatological Institute imeni N. A. Semashko]

UDC 616-001.28-089.22:612.342.4

[Abstract] Experimental therapeutic trials were conducted on the management of wounds with trypsin immobilized on gauze and capron dressings vis-a-vis conventional management without enzymatic debridement. The study was performed on 3 kg chinchilla rabbits with subacute radiation sickness following 7 Gy gamma irradiation, bearing a 3 cm diameter full-thickness surgical skin wound infected with E. coli. Histologic and bacteriologic monitoring demonstrated a more rapid healing and formation of granulation tissue in the trypsin group with the dressings changed q. 72 h, with the capron dressing shown to be more effective. In addition, fewer microabscesses and bacterial colonies were encountered in the trypsin group. On day 8 an inflammatory rebound phenomenon was noted in the control rabbits, whereas healing was proceeding unabated in the experimental rabbits. On balance, the results showed that treatment with trypsin immobilized on gauze and, especially, capron promoted more rapid wound healing in rabbits with subacute radiation sickness and facilitated elimination of E. coli. References 6: 4 Russian, 2 Western.

Change of Emission Spectra of Acridine Orange Stained Blood Cells of Lymphosarcoma and Leukemia Patients in Process of Chemotherapy

917C0560A Kiev EKSPERIMENTALNAYA ONKOLOGIYA in Russian Vol 13 No 2, Mar-Apr 91 pp 50-53

[Article by N. A. Karnaukhova; Institute of Biological Physics; USSR Academy of Sciences; Pushchino]

UDC 535.37:616-006.44

[Abstract] A study of bone marrow and peripheral blood of 25 patients with lymphosarcoma and leukemia before and in the process of chemotherapy involved placement of patients, after chemotherapy, in one of three groups: group 1 patients responded to chemotherapy and experienced remission; group 2 patients experienced little benefit from chemotherapy and most of them died; group 3 patients included those for whom a shift into group 1 or group 2 could be predicted with reasonable probability. Thus, changes of the emission spectrum of the blood cells helped in predicting the effectiveness of the chemotherapy and made it possible to select appropriate treatment or to correct the procedure being performed. Figures 6; references 15: 14 Russian, 1 Western.

Effect of Polymer Composition Containing Levamisole on Growth of Sarcoma 45 in Rats

917C0560B Kiev EKSPERIMENTALNAYA ONKOLOGIYA in Russian Vol 13 No 2, Mar-Apr 91 pp 59-62

[Article by N. A. Galatenko, V. A. Baraboy, B. A. Tolstopyatov et al.; Kiev Scientific Research Institute of Oncology; UkSSR Ministry of Health; Institute of Organic Chemistry; UkSSR Academy of Sciences; Kiev]

UDC 616.006.188-003.93:612.018

[Abstract] A study of inhibition of growth of sarcoma 45 and changes of morphological features in rats after local effect of a polymer (polyurethane) composition containing levamisole (6 percent) followed subcutaneous transplantation of sarcoma 45 cells into 294 mongrel male rats weighing 200-220 g. The procedure produced local activation of the immune link, including macrophagic elements.

intensified the growth of granulation and inhibited tumor growth. The study showed complete tumor regression in 68 percent of the cases. Figures 1; references 14: 11 Russian, 3 Western.

Antitumoral Activity of Liposome-Encapsulated Cortiphen Injected Into Mice With Solid Tumors

917C0560C Kiev EKSPERIMENTALNAYA ONKOLOGIYA in Russian Vol 13 No 2, Mar-Apr 91 pp 65-67

[Article by V. I. Kaledin and Yu. N. Kurunov; Institute of Cytology and Genetics; USSR Academy of Sciences; Siberian Department; Novosibirsk; Novosibirsk State Medical Institute]

UDC 616.006:615.277.3

[Abstract] Production of encapsulated cortiphen and comparison of its effect after injection into mice with solid tumors with the effect of free cortiphen involved experiments on 267 four- to six-month old A/He and C3HA mice with use of the line-specific Krebs 2 tumor and GA-1 tumor of hepatic origin. Transplantation of 0.5-1.0 million tumor cells into the thigh preceeded injection of encapsulated cortiphen and free cortiphen into mice with Krebs carcinoma by three days and into mice with GA-1 tumor by 13 days. Liposome-encapsulated cortiphen equalled free cortiphen in antitumor activity and sometimes surpassed it. The possibility of systemic use, simplicity of preparation and the capacity to endure liophilic drying make liposome encapsulated preparations a possible alternative medicinal form for antitumor hormone cytostatics, especially cortiphen. Figures 1; references 7: Russian.

Effects of Lyophilization and Storage Conditions on Viability of Bacterial Pathogens of Rice

917C0501A Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 52 No 6, Nov-Dec 90 (manuscript received 23 Aug 89) pp 7-12

[Article by Ye. V. Matveyeva, G. K. Samokhvalova, M. A. Odintsova, A. S. Kaprelyants and B. N. Kulikov, All-Union Scientific Research Institute of Phytopathology; Institute of Biochemistry, USSR Academy of Sciences, Moscow]

UDC 579.083.13

[Abstract] Optimum conditions for lyophilization and preservation of the important rice pathogens Xanthomonas campestris, Pseudomonas syringae and Ps. fuscovaginae were determined. The results demonstrated that highest retention of viability was obtained when the bacteria were lyophilized in the following medium: 1 percent gelatin + 10 percent sucrose + 0.5 percent thiourea. Subsequent storage at < 5°C in vacuo with residual moisture content of ca. 3.5 percent assured the highest levels of viability (71.6-90.6 percent). In addition, an inverse relationship was demonstrated between storage temperature (-20 to +20°C) viability. Figures 1; tables 4; references 11: 6 Russian, 5 Western.

Production and Description of Nonencapsulated Yersinia Pestis

917C0501B Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 52 No 6, Nov-Dec 90 (manuscript received 20 Jun 88) pp 13-17

[Article by N. A. Gvozdenko, V. Yu. Ryzhkov and N. V. Pavlovich, Rostov-on-Don Scientific Research Antiplague Station]

UDC 579.842.23.25

[Abstract] Several methods were tested for the production of nonencapsulated Yersinia pestis strains from wild Fra^+ strains, including (1) cultivation in broth LB pH 7.1 in the presence of 1 percent specific agglutinating antiserum, (2) treatment with nitrosoguanidine, and (3) cultivation in the presence of acridine orange and novobiocin to eliminate plasmid Fra1/Tox (65 MDa; encoding capsule formation). Method 1 was found to be the most efficient process for producing Y. pestis Fra^-, yielding 15 mutants. Eight of the nonencapsulated mutants retained high virulence for albino mice (LD_{50} = 10-178 bacterial cells), four mutants showed diminished virulence (LD_{50} = 3162 cells), and three were avirulent (LD_{50} = 10E9 cells). Electrophoretic determinations demonstrated that loss of the ability to synthesize a capsule was not due to loss of the Fra1/Tox plasmid, but to a mutation in the encoding gene. Reversion to the Fra^+ status on storage on synthetic media or via animal passage as a result of derepression required presence of the Fra1/Tox plasmid. Tables 1; references 12: 10 Russian, 2 Western.

Selective Immobilization of Metalloenzymes of Acremonium Chrysogenum Multienzyme Complex on Silica Gel

917C0501C Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 52 No 6, Nov-Dec 90 (manuscript received 24 Oct 89) pp 24-29

[Article by S. V. Sokol, L. I. Kiseleva, I. F. Mishunin and I. M. Samodumova, Institute of Biochemistry, Ukrainian SSR Academy of Sciences, Kiev]

UDC 577.151.62

[Abstract] A method was devised for immobilization of the metalloenzymes of a proteolytic multienzyme complex of Acremonium chrysogenum on silica gel, based on Co(II)-dependence of the amino- and carboxypeptidase components. Selective immobilization of the metalloenzymes was obtained by mixing Co ion-free enzyme complex with Co(II)-silica gel. Co(II)-silica gel was prepared by mixing sodium silicate + sulfuric acid + cobalt chloride, while Co ions were eliminated from the enzyme active site by pretreatment of the complex with EDTA for 16 h at 4°C. Determinations of enzyme activities showed that ca. 90 percent of the carboxypeptidase and 62 percent of the aminopeptidase was immobilized after 60 min at 23°C in 0.05 M tris-HCl buffer, pH 7.8. After three cycles of use the immobilized enzymes retained 70 percent of the initially bound carboxypeptidase activity and 95 percent of the aminopeptidase activity. Figures 5; tables 1; references 18: 7 Russian, 11 Western.

Production of Exopolysaccharides by Mixed Cultures on Ethanol Substrate

917C0501D Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 52 No 6, Nov-Dec 90 (manuscript received 6 Feb 90) pp 30-34

[Article by T. A. Grinberg, T. P. Pirog, S. M. Suprun, V. N. Buklova, L. A. Zakordonets and Yu. R. Malashenko, Institute of Microbiology, Ukrainian SSE Academy of Sciences, Kiev]

UDC 579.222

[Abstract] Culture conditions were assessed to insure maximum exopolysaccharide (EPS) production by an auxotrophic Acinetobacter sp., which included utilization of mixed cultures. The results showed that maximum yields of EPS of 2.9-3.0 g/L were obtained with the combinations of Acinetobacter sp. + A. calcoaceticus (3:1 cell ratio) and Acenetobacter sp. + Fusarium sp. (4:1) after 72 h of growth at 30°C on Kodama's medium supplemented with 1 percent ethanol as the carbon source and NH_4NO_3 or NH_4Cl as the nitrogen source. In addition, EPS levels of 2.12 g/L were obtainable when the producer was cultivated in a medium supplemented with the supernatant from a 24 h Fusarium sp. culture. Since the Fusarium may also be used as a single-cell protein, such a two-stage process ensures an essentially waste-free biotechnological process. Figures 1; tables 3; references 10: 1 Ukrainian, 6 Russian, 3 Western.

Aspartate/NMDA-Sensitizing Effect of Piracetam

917C0486 Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 316 No 2, (manuscript received 25 Jul 90) pp 501-503

[Article by I. V. Komissarov, I. I. Abramets, and I. M. Samoylovich, Donetsk Medical Institute imeni M. Gorkiy]

UDC 612.82/612.83+591.482

[Abstract] Piracetam is shown to potentiate the effects of glutamate and aspartate at the allosteric glycine-regulated sites of NMDA-receptors. Half of an *R. esculenta* frog spinal cord dissected in the sagittal plane, with the ventral and dorsal radices preserved, is placed in a 0.5 ml chamber superfused with either a saline solution containing various amounts of sodium chloride, potassium chloride, sodium phosphate, magnesium sulfate, and glucose or the same solution free of Mg^{2+}; solution temperature was 18-20°C. Standard microelectrodes recorded membrane potential changes and motor-neuron membrane resistance. It was established that *L*-glutaminic acid and *L*-aspartic acid, when brought into contact with motor neurons, result in a depolarization whose magnitude fluctuates between a few millivolts to 20 mV, with averages of 13.2 + 1.4 mV and 11.2 + 1.3 mV. In most of the neurons, the depolarization is accompanied by a reduction in membrane input resistance of 10-30 percent. Depolarization took place in both saline solutions. Predominate *L*-aspartic acid activation of NMDA receptors in the magnesium-free solution was confirmed by the fact that the aspartic-acid evoked depolarization responses of the motor neurons were suppressed in the presence of ketamine, but were enhanced by glycine. Like glycine, piracetam amplifies the effects of *L*-aspartic acid, with the increase in depolarization responses to the application of aspartic acid achieved in the presence of 100 µmol/l piracetam. The researchers feel justified in concluding that piracetam's ability to facilitate interhemisphere transfer may be the result of piracetam's glycine-like allosteric elevation of NMDA-receptor affinity to excitatory amino acids. In light of the role of those receptors in postsynaptic potentiation, piracetam's ability to eliminate the amnestic effect of proline, and the similarity of the molecular substrates of their action, piracetam's nootropic effect may be the result of its NMDA-sensitizing properties. Figures 2; references 14: 2 Russian, 12 Western.

Comparative Analysis of Nerve Growth Factors Via Use of Computer

917C0490A Tashkent DOKLADY AKADEMII NAUK UZSSR in Russian No 11, Nov 90 (manuscript received 20 Jul 90) pp 53-55

[Article by I. I. Parilis, R. S. Salikhov, D. B. Mirkhodzhayev, Ye. Yu. Kazanov, L. Ya. Yukelson, and UzSSR Academy of Sciences Academician D. Kh. Khamidov, Institute of Biochemistry, UzSSR Academy of Sciences]

UDC 575.321:598.12

[Text] At present, a great deal of information exists on the amino acid composition and primary structure of a great many proteins and polypeptides.[1] That information, which makes up various data banks, can be used for studying the evolution of proteins, for determining higher levels of their structure, and explaining the structural bases of their biological function. The basic approach involves comparing proteins that are homologous in structure or function, and that comparison is performed with special mathematical and computer techniques.

Mathematical programs that we developed can be used to analyze the phylogenesis of toxic components by means of a comparison of their amino acid sequences.[2] The greater degree of access to experimental data pertaining to the amino acid compositions of proteins and polypeptides has prompted researchers to develop programs for comparing the amino acid compositions. We developed such programs and were successful in using them for polypeptides with neurotoxic and cytotoxic functions.[3,4] This paper presents the results of a computer analysis of the amino acid composition of proteins with nerve growth activity (NGF) in mice (M), humans (H), bulls (B), chickens (C), snakes (S), and frogs (F). The amino acid compositions and sequences for the first five proteins are known from the literature, and the amino acid composition of the frog NGF was ascertained by us recently. A common feature of all the NGFs that were compared is a low content of apomatic amino acids, with the content of other amino acids varying.

To reconstruct a model of the process of evolution and to construct the phylogenetic tree, it is necessary to determine either the mutational paired distances between the proteins[2] or other values that correlate with those distances.[3,4] Since the primary structure of the frog NGF is not determined, for the entire group of proteins under study we calculated:

—(1) the Euclidean distance d_e with the formula

$$d_e(i, j) = \sqrt{\sum_{k=1}^{18} (C_{ik} - C_{jk})^2},$$

where i and j are the numbers of the proteins (in our case, they were 1-6), and C_{ik} and C_{jk} are the content (in percent) of each amino acid in the proteins, where k varies from 1 to 18;

—(2) the correlation distance d_k, in which the correlation coefficient $R(i, j)$ between the amino acid compositions of the proteins being compared (i, j) is the measure of proximity of the proteins; that distance is calculated with the formula:

$$d_k(i, j) = 100\text{-}100\ R(i, j).$$

Figure 1 presents the calculated Euclidean distances in pairs for all the proteins under study. The closest proteins are those with the smallest distance value, which signifies that they and the corresponding organisms diverged as the

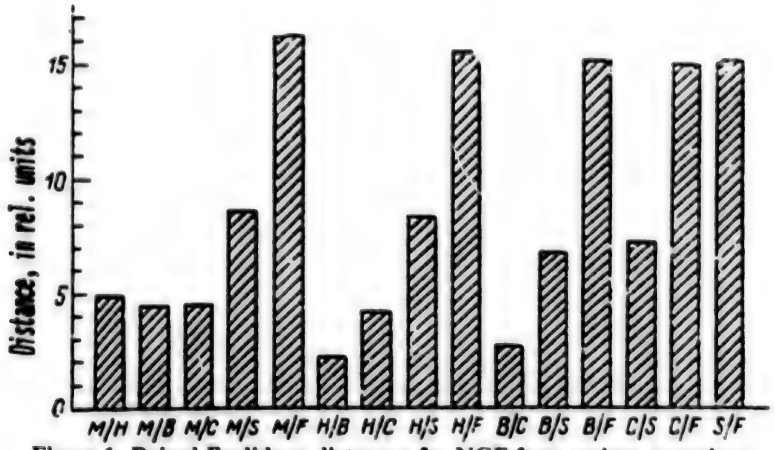


Figure 1. Paired Euclidean distances for NGF from various organisms

organisms evolved. That pertains primarily to the pair human/bull (H/B), whereas they are farthest apart in the pair mouse/frog (M/F).

Using an algorithm for consolidation from the assumption of uniform rate of accumulation of mutations, one can construct the proper phylogenetic tree (Fig. 2).

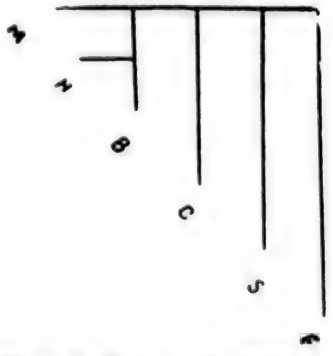


Figure 2. Phylogenetic NGF tree

Based on the program we have developed, a computer testing technique has been proposed that enables one to determine to which group of proteins the object under study belongs. Computer testing of the NGF from muscles of the lake frog in a number of other NGF proteins and proinsulins close to them confirmed that the NGF indeed belongs to a group of proteins with nerve growth activity.

References

1. Dayhoff M. O. "Atlas of Protein Sequence and Structure." 1972, Vol 5; 1973, Suppl 1; 1979, Suppl. 2, 3. Washington, D. C: National Biomed. Ras. Foudation [*sic*].

2. Paralis I. I., Bussel G. L., Yukelson L. Ya., Khamidov D. Kh. DOKL. AN UzSSR, 1984, No 10, pp 47-49.

3. Paralis I. I., Bussel G. L., Yukelson L. Ya., Khamidov D. Kh. MOL. BIOL., 1988, No 6, pp 1696-1701.

4. Yukelson L. Ya., Paralis I. I., Bussel G. L., Khamidov D. Kh. KHIMIYA PRIROD. SOYEDIN., 1989, No 6, pp 822-830.

Simple Ethers of the Alkaloid Lupinine: Synthesis and Cholinergic Activity

917C0490B Tashkent DOKLADY AKADEMII NAUK UZSSR in Russian No 11, Nov 90 (manuscript received 21 Feb 90) pp 29-30

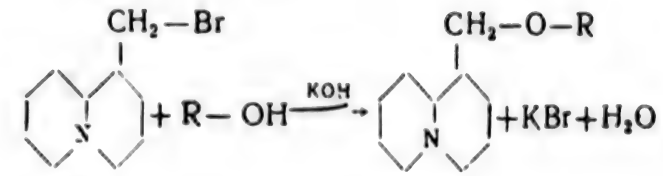
[Article by UzSSR Academy of Sciences Corresponding Member A. A. Abduvakhabov, R. T. Tlegenov, Z. Tilyabayev, Kh. Khaitbayez, D. N. Dalimov, and K. U. Uteniyazov, Institute of Bioorganic Chemistry imeni Academician A. S. Sadykov, UzSSR Academy of Sciences]

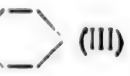
UDC 547.94.577.15

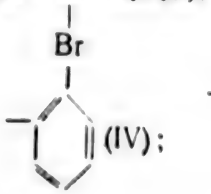
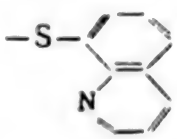
[Text] The introduction of various radicals into the structure of cholinotropic substances of natural origin can considerably affect their interaction with cholinergic systems of living organisms.[1]

Certain esters of lupinine and epilupinine are known to have cholinesterase activity. Depending on the structure of the acid portion, they have been either substrates or reversible inhibitors of two types of cholinesterases.[2] In continuing the study in that direction, we found it of interest to determine what kind of cholinesterase activity there would be with derivatives of lupinine that do not have an ester grouping, but an ether grouping. Since the literature contains no information on the effect that such

compounds have on the catalytic properties of cholinesterases, we synthesized[3] ethers of lupinine with a profile



где R: $H_3C-\underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{C}}-C_4H_9$ (I); $-CH_2-CH_2N(C_2H_5)_2$ (II);  (III)

 (IV);  (V);  (VI).

Compound	n_D^{20}	R_f	Yield, %	Iodomethylate, melting point, °C	$K_i \cdot 10^{-5}$, M	
					AChE	BChE
I	1,3680	0,29	70	255–258	3,65	1,3
II	1,3735	0,40	68	194–196	1,65	0,61
III	1,3620	0,54	66	135–137	3,48	15,7
IV	1,5970	0,36	50	246–248	2,08	20,8
V	—	0,39	45	Гигр.	1,68	0,70
VI	1,4592	0,28	78	167–169	4,17	4,46

Physical and chemical characteristics and reversible inhibitory activity of lupinine ethers

Substances that were produced by the action of methyl iodide were converted into the corresponding iodomethylates, whose physical and chemical characteristics are presented in the table.

The iodomethylates of the lupinine ethers were studied in reactions involving interaction with acetylcholinesterase (AChe) and butylcholinesterase (BChE) of warm-blooded animals.

Experiments to determine the effect of the ethers on the enzyme properties of the cholinesterases with the Ellman colorimetric technique (at 25°C, pH 7.5).[4] The results of the effects of the ethers are summarized in the table, and from them it follows that all the compounds studied reversibly (in the concurrent-mixed type) slow the catalytic activity of AChE and BChE. The inhibitory efficiency of the compounds was judged from the magnitude of the total inhibitory constant K_i, defined graphically in the coordinates $1/v$ from $1/s$.[5]

In activity, some ethers considerably exceed the typical reversible inhibitors, which are alkylammonium ions. In inhibitory activity, substances II and V are the strongest inhibitors for AChE. Substances I and III showed identical activity for that enzyme. However, their efficiency was lower than that of II and V by more than a factor of 2. AChE sensitivity to compound VI was especially low.

The sensitivity of BChE to those compounds differed from that of AChE. Substances II and V were the strongest effectors of BChE. Their activity in relation to BChE was identical, although, looking at the table, one may notice that the blocking capacity of compound V, which has a bulky oxycholine residue, is somewhat higher. Compounds III and IV are the weakest BChE inhibitors. It should be noted that for AChE, those compounds have only medium strength, as compared with the other ethers. The results confirm the fact established earlier[6] that hydrophobic interaction is more typical in BChE interaction with effectors than is ion-ion interaction.

The study of the anticholinesterase properties of the ethers that were produced showed that they interact with the active surface of the enzymes, as do the esters produced earlier, forming sorption enzyme-inhibitor complexes. The ability of the compounds to inhibit both enzymes depends on the degree of correspondence between the structure of the synthesized ethers and the structure of the active surface of AChE and BChE.

References

1. Abduvakhabov A. A., Sadykov A. A., Dalimov D. N., Aslanov Kh. A. "Alkaloidy i ikh proizvodnyye kak instrument flya izucheniya kholinergicheskoy sistemy" [Alkaloids and Their Derivatives As an Instrument for Studying the Cholinergic System]. Tashkent: Fan, 1984.

2. Abduvakhabov A. A., Kasymov Sh. K., et al. DOKL. AN SSSR, 1975, Vol 220 No 4, p 961.

3. Sadykov A. S. "Khimiya alkaloidov Anabasis aphylla" [Chemistry of Anabasis aphylla Alkaloids]. Tashkent: Izdvo AN UzSSR, 1956, pp 192-194.

4. Ellman G. L., Courtney R. D., Anders V., Featherstone K. M. BIOCHEM. PHARMACOL., 1961, Vol 7, p 88.

5. Brestkin A. P., Vinyar. T. N., Rozengart Ye. V. BIOKHIMIYA, 1981, Vol 46, pp 1042-1048.

6. Kabachnik M. I., Abduvakhabov A. A. et al. USPEKHI KHIMII, 1970, Vol 39, pp 1050-1073.

Impact of Hepatic Regeneration on Mitochondrial Energy Metabolism in Diffuse Liver Damage in Rats

917C0500B Yerevan EKSPERIMENTALNAYA I KLINICHESKAYA MEDITSINA in Russian Vol 30 No 5, Sep-Oct 90 (manuscript received 18 Jul 89) pp 461-467

[Article by A. S. Dzhavadyan, T. D. Karapetyan, S. S. Gambarov, I. R. Saakyan, V. S. Petrosyan and A. L. Bagdasaryan, Yerevan Branch, VNTsKh [expansion unknown], USSR Academy of Medical Sciences]

UDC 616.36-001.003.93

[Abstract] Trials were conducted on outbred male rats (250-300 g) to assess the effects of partial hepatectomy and partial two-stage spleen resection in combination with myelopid administration (0.5 mg/kg, i.v.) on mitochondrial energy metabolism in diffuse liver damage. The latter was induced by long-term geliotrin [sic] administration. In the case of control animals the combination of surgical procedures and myelopid enhanced mitochondiral energy metabolism and led to depletion of respiratory chain reserves. In the cases of hepatopathology the mitochondria were hypometabolic and characterized by a prolonged phosphorylation time. Combined therapy resulted in more efficient energy metabolism and much shorter phosphorylation times leading to improved energy reserves. Consequently, these results indicate that the level of mitochondrial energy metabolism may be used as an indicator of therapeutic efficacy in diffuse liver damage. Figures 2; tables 1; references 14: 9 Russian, 5 Western.

Myelopid Effects on Ultrastructure and Dry Weight of Alveolar Cells in Endotoxin-Treated Rats

917C0500D Yerevan EKSPERIMENTALNAYA I KLINICHESKAYA MEDITSINA in Russian Vol 30 No 5, Sep-Oct 90 (manuscript received 17 May 89) pp 477-483

[Article by E. A. Bardakhchyan and N. G. Kharlanova, Rostov Scientific Research Antiplague Institute; Rostov Medical Institute]

UDC 616.24-073.75:599.323

[Abstract] Shock lung was induced in 200 g albino rats by E. coli endotoxin administration (2 mg/100 g, i.v.) to test the efficacy of myelopid in preventing the endotoxin-mediated pulmonary pathogenesis. The combination of ultrastructural and cytointerferometric studies demonstrated that pretreatment of the animals with myelopid (0.3 mg/100 g, i.p.) 24 h before endotoxin administration prevented or markedly attenuated swelling of type I alveolar cells, atelectasis, and rheologic abnormalities and microvascular pathology. In addition, myelopid prevented reduction in lamellar bodies in type II alveolar cells, facilitated proliferation and activation of plasma cells and enhanced phagocytic activity of alveolar macrophages. Figures 1; tables 2; references 13: 10 Russian, 3 Western.

Nutritional Status in Rural Areas in Armenia

917C0500A Yerevan EKSPERIMENTALNAYA I KLINICHESKAYA MEDITSINA in Russian Vol 30 No 5, Sep-Oct 90 (manuscript received 15 Oct 89) pp 407-412

[Article by P. A. Bakalyan, O. A. Antonin, R. A. Matevosyan and L. G. Oganesyan, Chair of Hygiene, Sanitary Hygienic Faculty, Yerevan State University]

UDC 613.2(-22)(47.925)

[Abstract] The nutritional status of 5,007 subjects in nine rural rayons in Armenia was assessed in objective and subjective terms in order to determine the need for possible modifications in nutrition policy and health education. The results revealed that the daily caloric intake was on the order of 3008 kcal, consisting of an adequate intake of carbohydrates (370.9 g), somewhat elevated intakes of proteins (102.9 g vs. recommended 90 g) and fats (124.8 g vs. 110 g). The intake of essential amino acids is normal, despite the fact that animal proteins account for 42.2 percent of the protein intake versus the 55 percent recommendation. However, animal fats represented an excess (80.1 percent) over vegetable fats. In general, the protein:fat:carbohydrate ratios stood at 1:1.2:3.6 instead of the recommended 1:1.2:4.6. Intake of magnesium and phosphorus exceeded recommended values, while calcium intake was below the norm, and intake of iodine and fluoride was considerbly below normal. Vitamin intake was generally within accepted norms, although the intake of vitamin A was 3-fold below and vitamin B-2 1.5-fold lower than recommended levels. On balance, rural nutrition was found to be satisfactory for low levels of activity, but inadequate in seasons requiring greater expenditures of energy. Accordingly, these findings indicate that there is room for improvement in the rural nutrition policy in Armenia. Tables 2; references 6: Russian.

Insured Medical Care: Realities and Prospects

917C0554C Alma-Ata ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian No 2, Feb 91 pp 16-19

[Article by S. N. Arystanova, P. P. Petrov, M. K. Kulzhanov and L. S. Sultangaliyeva, Ministry of Health, Scientific Research Institute of Hygiene and Occupational Diseases, Alma-Ata]

UDC 614

[Text] Public health is one of the most important factors promoting successful implementation of social policy. The legal principles of public health are expressed in the Constitution. The state's planned efforts in public health rely upon economic laws. However, the crisis that has matured in recent years in the country's national economy compels us to reevaluate the established relationships between the economy and public health, and many of the priorities.

The republic's transition to cost accounting and self-financing forces us to seek new approaches to solving the problems of protecting and preserving the health of the people, and in the shortest time possible at that. We are facing the need for making all elements of the republic's national economy economically interested in strengthening the health of the people. Concurrently, we are also faced by the task of raising the material responsibility of each member of the society for improving his own health. One of the ways of attaining this goal is to create a situation in which it would be economically disadvantageous for enterprises to manufacture products that are detrimental to the health of the people.

The search for new sources of public health financing compels us to also take a fresh look at the existing insurance system, which puts enterprises with higher morbidity in a more advantageous position, since the wage fund savings of such enterprises are also high. On the other hand the present system provides no stimuli for preserving the health of workers, since this would require sizable allocations to improve working conditions, modernizing production, and organizing healthy leisure time and rest for workers.

Economic and moral stimuli are also assuming priority. Their implementation should promote formation of a medical worker of a qualitatively new type, one whose professional training would satisfy current needs. Life is changing the doctor-patient relationship: Now the latter is able to choose the doctor by whom he wishes to be treated. The hospital-polyclinic link, which was inseparable just yesterday, is also breaking. Under that system, the patient is totally at the mercy of the section physician not only at the outpatient and polyclinic level but also in the hospital.

Social injustice is also compounded by the existence of social consumption funds, which in reality redistribute the people's money in an uncontrolled manner. Also having an effect is the unfortunate residual principle of financing public health, which receives only 3 percent of the national income through the budget.

Given the present conditions, it would seem best to convert to the principles of insured medical care, which would provide a possibility for public health and social welfare to function independently. The new financing model we propose integrates public health into the monetary flows of expanded reproduction. While in former times money flowed "from the bottom up and then down," in the system proposed here it will flow predominantly in a horizontal direction.

The new model calls for combined financing of public health by the budget and through insurance payments. The system is based on a balanced combination of budgetary and nonbudgetary sources of assets, coupled with noticeable decentralization of the sector's finances in favor of self-managed territorial programs. The model also presupposes more specific accumulation of resources in support of medical care.

The most important principle of organizing medical insurance is dominance of group insurance as mandatory over voluntary individual insurance supplementary to it. The main objects of insurance are the following population groups:

—labor collectives with different forms of ownership (state, kolkhoz, cooperative, joint-stock, private etc.);

—retired persons;

—young university and trade school students;

—large families;

—the unemployed;

—socially deprived categories of the population.

The procedure by which insurance is provided to each individual population group on this list is differentiated with respect to financing sources. At the same time, provision of insured medical services is established for all citizens of the country at a level not below those services that are socially necessary. As a result the universality of medical insurance is assured as the fundamental principle of a socially just system.

Public health continues to be financed by the budget at unchanged volume; however, this financing is more purposeful, controlled and stable, inasmuch as the bulk of the assets are allocated not from the budget's total income but rather from an independent fund, on the basis of standards on budgetary allocations to state medical insurance.

Moreover the public health budget will be supplemented by monetary income from penalties, from money in the budget not spent on public health in the previous year, from profit from therapeutic, economic and commercial activity, and a fraction of the turnover tax from the sale of products harmful to the population's health.

Nonbudgetary sources of public health financing will include mandatory payments by enterprises and organizations into territorial medical insurance funds. Such payments are established in the form of preferential taxation of enterprise profits. The level of such taxation may be established as a standard of the wage fund (from 4 to 9 percent).

In the next five to seven years, payments for medical insurance may be transferred steadily to product cost. Gradual inclusion of these payments into product cost will make it possible to avoid an inflation spiral in the national economy which may result from an immediate transfer of a sizable fraction of the additional expenses on public health to the cost-accounting economy.

Setting the insurance rates is an important step. The rate is initially set to be the same for the entire country, and in the future it is differentiated in relation to different territories, regions and objects of insurance. Factors that would shift the rate from its base level would include:

1. The state of the environment. In ecologically unfavorable regions, where morbidity is higher as a rule, territorial medical insurance funds must concentrate relatively larger assets per insured individual. Consequently the enterprises would also be obligated to deduct assets at a higher rate. However, this rule would apply only to those enterprises which contribute by their action to worsening of the environment.

In regions of ecological disasters (the Sea of Aral, Balkhash, Semipalatinsk Oblast, Eastern Kazakhstan and elsewhere), where significantly greater assets are required to restore the environment and the health of the population, the government and the ministries and departments responsible for development of such a situation provide additional assets to the given territory.

2. The quality of the production environment at the enterprise. The scale of manual and physically heavy labor, the amount of noise and chemical contamination in the shops, and presence of constant mental and emotional stresses affect morbidity and health. In this case the enterprise increases its insurance payments by contributing more of its own assets.

3. The social and demographic composition of the population. The greater the proportion of population categories such as retired persons, disabled persons, juveniles and indigents in the total number of residents within the given region, the greater the financial load borne by local enterprises in developing universally available medical insurance should be.

4. The assortment and volume of therapeutic and preventive services covered by medical insurance. Besides multipurpose medical insurance funds that provide compensation for the entire complex of therapeutic and preventive services, insurance funds that specialize in relation to particular forms of services and population groups may be created. In this case the profile of the activity of the corresponding territorial fund becomes a factor in the differentiation of insurance rates.

It should be emphasized that territorial medical insurance provided by an enterprise is group and not individual insurance. Medical insurance payments made for a "healthy" individual will be used in part in support of a "sick" one. Such is one of the manifestations of the principle of social solidarity, which cements together the given system of specific-purpose social insurance. In our case this principle is all the more justified because it is realized through the enterprises, such that medical care for the population remains free.

The demand of some socially unprotected population groups for medical care will be calculated below with regard for change in the manner of allocation of budgetary assets. These groups include retired persons, large families, university students and workers of budget-supported organizations.

According to the results of our research, pensioners will require public health services totaling R142 per year. Knowing the number of retired and disabled persons in the republic, and the standard level of consumption of medical services by them, we can calculate annual expenditures in a medical insurance program. According to our calculations they may total R300 million per year.

There are around 1 million children being raised in large families in the republic. Expenditures on this contingent of

the population may total around R140 million. The financial program for young university and trade school students is calculated in similar fashion.

Concern for workers of budget-supported institutions is another responsibility that should be laid upon the state medical insurance fund. According to our estimates such workers make up about 35 percent of the number of persons employed in the national economy, who together with their families total around 6 million persons. The cost of providing medical care to this contingent will be around R280 million.

The financial program of state medical insurance concerned with financing science, education, the epidemiological service and capital investments will be approximately 7.0, 62.0, 42.0 and 92.0 million rubles respectively.

Territorial medical insurance funds will be created out of deductions from the profits of enterprises and organizations. The insurance rates may be established, depending on work effectiveness and profitability, from 4 to 9 percent of the wage fund. For example when the rate is set at 4 percent, deductions into the territorial insurance fund may total R737 million, while at a rate of 9 percent they would be R1.6 billion.

There are 1.2 million persons in the republic employed in cooperatives and in private business. The insurance payments of this category of the population will total R55 million.

Thus the system proposed here for forming medical insurance funds out of different financing sources can provide for a one-time increase in the national public health budget of the Kazakh SSR to R2.7 billion assuming a 9 percent insurance rate; in other words a more than 2-fold increase will be assured.

Association of Leasing Polyclinics—A New Form of Their Management

917C0570A Moscow SOVETSKOYE ZDRAVOOKHRANENIYE in Russian No 3, Mar 91 pp 20-24

[Article by I. V. Polyakov, G. V. Zavarina, O. V. Samovarova and K. V. Ponomareva, Leningrad Financial-Economic Institute imeni N. A. Voznesenskiy]

UDC 616-082:658.387

[Text] Along with the fundamental changes occurring in budget financing of public health institutions, active use of all forms of cost accounting and of various forms of property ownership are required in the economic activities of public health institutions.

Research we conducted in a certain cost-accounting polyclinic of Leningrad shows that in order for polyclinics to become self-supporting, the increase in prices of certain items on the price list must be from 30 to 100 percent of the current price of services (in accordance with the presently operating expense mechanism of price setting). Considering that the cost of most paid services rendered by these polyclinics is within 1-3 rubles, we can suppose that after the price lists are reviewed, the prices of these services will not rise out of reach, and they will continue to be much lower than prices in medical cooperatives. On the other hand operation of paid polyclinics at a loss (with low profitability) contradicts the principle of cost accounting, retards development of the polyclinics and does nothing to improve their material and equipment base.

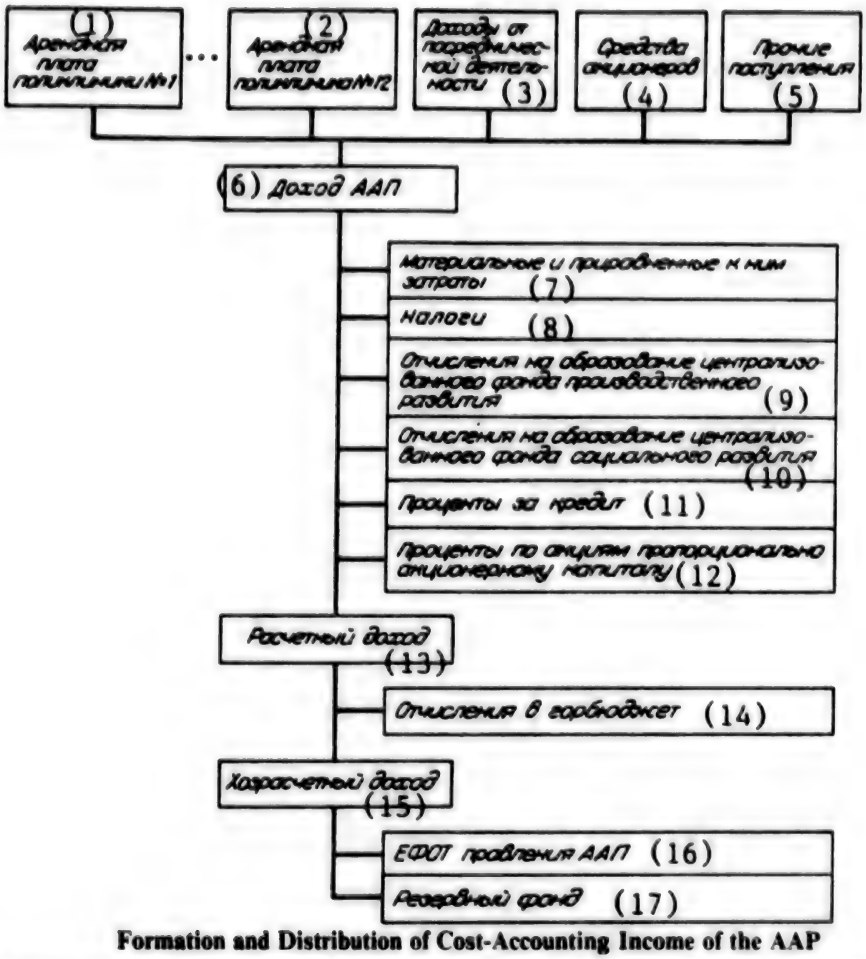
In this connection extensive introduction of cost accounting and of brigade and leasing contracts, and use and development of all forms of ownership in the absence of monopolies on medical services will make the "shadow economy" in public health unfeasible. According to certain estimates[1] its scale is R2-3 billion. According to data from a selective survey conducted by the Center for Public Opinion Research of the USSR Academy of Sciences Sociological Research Institute, 74.8 percent of the population seeks services from illegally paid physicians and physicians known on a personal basis.[2] This violates the principle of equal availability of medical services, and of course promotes redistribution of money not in favor of the development of the public health system.

Today, out of all existing forms of providing paid services, the only one that can realistically compete with cooperatives is cost-accounting polyclinics that have converted to leasing relations.

All of the above made it extremely important to evaluate the possibilities for converting Leningrad's cost-accounting polyclinics to leasing relations.

Economic models of formation and distribution of the cost-accounting income of polyclinics developed in 1989 by the authors of this article, models of internal leasing contracts at the division level, agreements on the economic and organizational principles of leasing relations of polyclinics with the Administration of Cost-Accounting Therapeutic Institutions (UKhLU), and statutes on their activities under leasing conditions made it possible to implement the principles of complete cost accounting—self-reliance, cost recovery and self-financing, and finally to have polyclinics live up to their name as cost-accounting polyclinics.

The agreement on the economic and organizational principles of leasing relations covers the entire system of mutual relations between the parties, to include mutual obligations, rights and responsibility. State orders provide the necessary volume of paid medical services to polyclinics for the time over which an agreement is signed. Cost-accounting income is used as the general indicator of a polyclinic's economic activity. This income forms as follows: First, all material and equipment expenditures and social insurance deductions are compensated and loan interest is paid out of the polyclinic's income, which leaves accounting income, from which lease payments are made according to the established procedure. Lease payments include part of the depreciation deductions, deductions to maintain the administrative staff of the polyclinics, and deductions to form centralized polyclinic production and



Formation and Distribution of Cost-Accounting Income of the AAP

Key: 1. Lease payments of polyclinic No 1; 2. Lease payments of polyclinic No 12; 3. Income from intermediary activity; 4. Shareholder assets; 5. Other income; 6. Income of the AAP; 7. Material and equivalent expenditures; 8. Taxes; 9. Deductions to form the centralized production development fund; 10. Deductions to develop the centralized social development fund; 11. Loan interest; 12. Interest on shares in proportion to joint stock; 13. Accounting income; 14. Deductions into the state budget; 15. Cost-accounting income; 16. YeFOT of the board of the AAP; 17. Reserve fund

social development funds. The polyclinic's cost-accounting income is distributed between the unified wage fund (YeFOT), the development fund and the reserve fund.

The leasing relations in the polyclinics we studied caused labor collectives and individual workers to become economically interested in increasing the volume and quality of services. For example, wages in one of the cost-accounting polyclinics that converted to leasing relationships as of January 1990 increased by 22 percent in one quarter. This was due, in large part, to the higher economic competency of polyclinic workers, who signed 20 contracts for medical services with various Leningrad enterprises immediately after converting to the new methods of management, in addition to providing services to the public.

Establishment of fundamentally new production relations between the bottom rung of the economic system—the polyclinics—and the top administrative subdivision—the UKhLU—makes it necessary to establish a new form of management of cost-accounting polyclinics operating on the basis of a leasing contract (we will refer to them as leasing polyclinics). This problem may be solved from our point of view by forming a Leasing Polyclinic Association (AAP). Considering the suitability of converting all Leningrad cost-accounting polyclinics to the new methods of management, the AAP may be formed out of the existing UKhLU, after reexamination of its functions. The need for uniting paid polyclinics (their number should subsequently increase) into their own association is dictated by presence of common organizational and economic problems, difficulties in the transitional period of conversion to leasing, weak development of their material and equipment base, and a lack of their own resources for development.

The objectives of the AAP should include not only hastening economic development of the system of paid medical services, but also substantially increasing their quality and quantity (through faster introduction of scientific and technical progress and the best experience, by raising culture and by using progressive forms of services and organization, and new types of services and so on).

The AAP should not be a substitute for or, all the more so, a hindrance to, development of the network of budget-financed public health institutions. But it will create conditions for competitive work by paid and free forms of medical services to the public. At the same time it provides the possibility for providing medical services more fully to all members of society under a system of voluntary payment.

Tentative calculations (ones of greater accuracy can be made only after conversion of all polyclinics to full cost accounting) show that the annual income of the AAP may be on the order of R410,000, of which 230 +/- 10 percent will be deducted annually into the Leningrad budget for public health needs (presently all of this money is absorbed by the state budget).

The principal objectives, rights, responsibilities and income distribution of the association should be reflected in a "Statute on the AAP" of approximately the following content.

I. General Provisions

1. The Leningrad AAP is a voluntary economic union of cost-accounting polyclinics providing paid services, the activity of which is directed at raising the effectiveness with which polyclinics are managed and increasing the quality and quantity of paid medical services. The association carries out its activity on the basis of normative acts, this statute, and decisions of a general assembly in interaction with state organs of administration.

2. In order to create new forms of interest and to increase the sense of ownership among its members, the AAP adheres to a policy of gradual transition of its property to collective and joint-stock ownership.

3. The association is a legal person possessing a clearing account in the bank, and a seal bearing its name.

In the interests of carrying out tasks and exercising powers established by the USSR laws "On the State Enterprise (Association)," "On Leasing" and "On Property Ownership," by existing legislation and other standards, statutes and acts, the AAP has a right to adopt all decisions at its own initiative to the extent that they do not conflict with existing legislation. The AAP bears full responsibility for observing the interests of the state and the rights of citizens, for safeguarding socialist property, for fulfilling adopted obligations and for making a profit.

II. Principal Objectives of the Association

1. Promoting the fullest possible reconciliation of the interests of members of the AAP and interests of the society on the basis of using progressive economic approaches and mechanisms.

2. Providing paid medical assistance to all members of the society desiring it, and ensuring equal rights of its acquisition.

3. Issuing state orders (a certain volume of medical services) to polyclinics and checking their activities in filling such orders.

4. Developing the principles of public medical insurance based on voluntary payment.

5. Carrying out intermediary functions in soliciting orders and forming a portfolio of orders by signing contracts with institutions and organizations for medical insurance and provision of medical services.

6. Providing polyclinics with information on the accomplishments of scientific and technical progress in public health, on the best experience, on standards, on advance training for personnel, and so on.

7. Studying market demand and creating demand for the principal forms of medical services in Leningrad and Leningrad Oblast.

8. Assisting polyclinics in solving problems arising with other departments.

III. Rights of the Association

1. To represent and defend the interests of members of the AAP, at their instructions, before the appropriate organs and organizations.

2. To lease fixed and productive capital to polyclinics (on the basis of rights delegated by the Leningrad City Soviet). To build, acquire and lease production space and other personal and real property in support of its activity.

3. To organize its affiliates and establish medical institutions and cooperatives according to established procedure.

4. To hire medical workers for second jobs based on wage contracts.

5. To reward members of the AAP and associates of the executive staff of the AAP who promote its successful activity.

IV. Membership and Responsibilities

1. Membership in the AAP is voluntary.

2. State and cooperative medical institutions providing paid medical assistance may be members of the AAP.

3. Members of the AAP are obligated: to promote attainment of the goals and objectives of the AAP; to observe the clauses of this statute and fulfill decisions of the executive organs of the AAP; to make prearranged lease payments or other deductions for which prior consent had been obtained.

4. Membership in the AAP is terminated: on the basis of a written statement submitted to the board of the AAP not less than three months prior to departure; as an exception, by a decision of the board for systematic violation of membership obligations and for indebtedness. The decision to expel may be appealed within a month's time.

V. Administration of the Association

1. The assembly of official polyclinic representatives, which convenes as necessary but not less than once a year, is the supreme administrative organ of the AAP.

2. In the period between assemblies, the AAP is administered by a board. The board is headed by a chairman elected for a five year term.

3. One representative from each member of the AAP participates in the general assembly.

4. An assembly is conducted with a quorum of not less than two-thirds of the votes, and decisions are based on majority rule.

5. The general assembly adopts the "Statute on the AAP" and amends it; it approves the basic directions and programs of the activity of the AAP; it approves the report of the board on the activity of the AAP; it determines the number of members of the board and the oversight council and appoints them for a term of up to five years; it examines complaints concerning decisions of the board.

6. The board of the AAP organizes fulfillment of decisions of the general assembly and reports to it; it approves the budget, the organizational structure and manning of the AAP; it accepts members into the AAP; it forms specific-purpose funds; it approves rules, resolutions and instructions concerning activities of the AAP; it adopts decisions pertaining to the acquisition, management and distribution of real property of the AAP; it resolves matters concerned with acquisition of stocks, and formation and distribution of joint stock; it performs other functions and responsibilities delegated by the general assembly.

VI. Assets of the Association

1. The AAP organizes its own activity on the basis of full cost recovery.

2. Decisions concerning expenditure of assets are adopted by the board.

3. Income of the AAP is the sum of deductions from lease payments to it by the polyclinics, which represent around 4 percent of their accounting income, income from intermediary activities, the assets of shareholders, and special dues paid by members of the AAP.

4. The AAP forms and distributes a centralized production development fund for members of the AAP for the purposes of developing and strengthening the material base of the polyclinics, and acquiring materials, working capital, modern equipment and so on; the AAP forms and distributes a centralized social development fund with the goal of creating its own sanatoriums, vacation bases, swimming pools, health clubs and so on.

6. An oversight council, which checks on the financial activities of the AAP and prepares reports for the general assembly and the board, is created to monitor expenditure of assets of the AAP.

7. In order to increase the interest of members of the AAP in creating new productive capital and develop a sense of ownership, part of the assets from the YeFOT and personal savings may be deposited in a special account. Attraction of the monetary assets of shareholders will create additional possibilities for development of the AAP. Formation and use of joint stock are governed by a special statute.

VII. Termination of the Activity of the AAP

1. The AAP terminates its activity by decision of the general assembly or the Leningrad City Soviet.

2. Assets from the sale of AAP property are transferred to the state budget following return of assets paid in on a proportionate basis.

This proposed AAP statute may be subjected to subsequent revisions, but the activity of its workers must be limited only to the functions listed here, and any interference in the economic activity of polyclinics that is not stipulated by agreement must be prohibited.

The success of radical restructuring of the economy of public health lies in a transition from administrative to economic methods of management, and it depends on the ability to determine and use sensible economic mechanisms. It is the initiation of one such mechanism that we attempted to illuminate in this paper.

Footnotes

1. LITERATURNAYA GAZETA, 3 February 1988.

2. IZVESTIYA, 14 January 1988. ©COPYRIGHT: Izdatelstvo "Meditsina", 1991

Some Social and Hygienic Aspects of Abortions in the Azerbaijan SSR

917C0570B Moscow SOVETSKOYE ZDRAVOOKHRANENIYE in Russian No 3, Mar 31 pp 32-34

[Article by F. B. Agayev and N. O. Mamedova, Azerbaijan Institute for the Advanced Training of Physicians imeni A. Aliyev of the Azerbaijan SSR Ministry of Health]

UDC 618.39-058-07 (479.24)

[Text] Abortions are a serious medical, social, moral and ethical problem [1,4,5,7-9]. In the USSR, the number of abortions significantly exceeds the number of successful pregnancies. The ratios between abortions and births differ significantly among the union republics. For example, there are 165 abortions for every 100 births in the RSFSR, and 27 for every 100 births in the Azerbaijan SSR. Maternal mortality associated with abortions also exhibits significant regional features [2,3]. Despite this, the social and hygienic characteristics of abortions have not been illuminated sufficiently in the literature, motivating us to study this problem with the Azerbaijan SSR as an example.

The study included women of child-bearing age, and information on their social and hygienic characteristics and the number and outcome of pregnancies was collected by questionnaire survey. Data on 1,073 women with a total of 2,457 pregnancies were used for analysis and statistical treatment. The material was subjected to statistical treatment with an IBM-PC personal computer. The results

showed that out of 1,000 cases of pregnancy, an average of 236.5 +/- 8.6 end in abortions, including 151.4 +/- 7.2 induced abortions (IA's) and 85.1 +/- 5.6 spontaneous abortions (SA's). According to official statistics the level of abortions was 212.5, which is an indirect indication that abortion records are incomplete. The ratio between IA's and SA's deserves special attention. According to our data more than a third of all abortions are spontaneous, which is an indication of significant shortcomings in the organization of preventive care for pregnant women. The proportion of SA's is especially high among housewives (50 percent) and women of Azerbaijani nationality (42 percent). The ratio between SA's and IA's varies significantly depending on the age of women. While abortions were predominantly spontaneous up to 20 years of age (64 percent), in subsequent age groups their proportion in the structure of abortions decreased, being 38, 36, 26 and 21 percent among women respectively 20-24, 25-29, 30-34 and 35 years and older. A strong direct correlation exists between the frequency of SA's and IA's as outcomes of pregnancy at a particular age. The parameters of this correlation are reflected in Table 1.

Table 1. Ratio of Pregnancies and Spontaneous and Induced Abortions Depending on Age of Women

Age Group	Number of Abortions per 1,000 Pregnancies		Parameters of Correlation Between Age and Nature of Abortions	
	IA	SA	IA	SA
Up to 20 years	32.9 +/- 14.5	59.2 +/- 19.1	r = 0.913	r = 0.935
20-24 years	124.9 +/- 10.2	79.1 +/- 8.3	m_r = 0.083	m_r = 0.062
25-29 years	162.1 +/- 12.6	94.7 +/- 9.7	t_r = 3.87	t_r = 4.562
30-34 years	246.4 +/- 25.7	89.2 +/- 17.0	a_1 = 13.665	a_1 = 1.781
35 and older	315.8 +/- 61.6	87.7 +/- 37.5	a_0 = 197.9	a_0 = 33.177
Total	151.4 +/- 7.2	85.1 +/- 5.6	d = 83.315	d = 87.401

Note: r—correlation coefficient; m_r—mean error of correlation coefficient; a_1 and a_0—regression level parameters; d—determination coefficient, percent; t_r—Student's test

Table 2. Ratio of Pregnancies and Spontaneous and Induced Abortions in Relation to Employment of Women in Social Production

Age Group, Years	Number of Abortions per 1,000 Pregnancies			
	Housewives		Working Women	
	IA	SA	IA	SA
Up to 20	24.1 +/- 16.8	84.3 +/- 30.5	43.5 +/- 24.5	43.5 +/- 24.5
20-24	59.8 +/- 12.4	97.8 +/- 15.5	145.4 +/- 13.5	60.2 +/- 9.1
25-29	112.4 +/- 53.4	106.4 +/- 19.4	135.8 +/- 13.2	111.9 +/- 12.2
30-34	281.7 +/- 53.4	84.5 +/- 33.0	244.0 +/- 29.7	81.3 +/- 18.9
35 and older	300 +/- 144.9	-	361.7 +/- 70.1	85.1 +/- 40.7
Total	96.0 +/- 10.5	96.0 +/- 10.5	155.7 +/- 8.8	83.5 +/- 6.7

Certain features were also revealed in the risk of SA's and IA's as pregnancy outcomes in relation to employment of women in social production (Table 2). The frequency of IA's is greater among working women. This is well expressed in ages up to 25 years. While the general levels of SA's are similar, differences are noted between housewives and working women of young age (up to 25 years), with the risk of SA's dominating among housewives.

The frequency and structure of SA's and IA's and their age dynamics among Azerbaijani women differed from the same indicators for women of other nationalities. Among Azerbaijanis, 119.5 +/- 7.2 out of 1,000 pregnancies ended in induced abortions, while for women of other nationalities this indicator was 336.5 +/- 23.2 ($p < 0.01$). In this case the frequency of SA's was similar in these groups at ages up to 20 years. A statistically significant difference in the level of SA's manifests itself in the group of women 20-24 years old, in which the number of abortions noted among Azerbaijanis and women of other nationalities was 77.5 +/- 8.9 and 327.0 +/- 37.2 abortions respectively per 1,000 pregnancies.

The literature contains conflicting information on the influence of preceding IA's on the risk of spontaneous interruption of pregnancy [1,2,6,10]. A study of the correlation between the level of SA's and IA's in different groups of women showed that it is not always statistically significant. For example in the group of women consisting of other nationalities, there was a strong direct correlation between the level of SA's and IA's, characterized by the following parameters: r = 0.78; m_r = 0.18; t = 2.46; d = 60.3. A regression equation by which to predict the level of SA's was constructed on the basis of this correlation:

Y = 0.2 +/- 0.083X,

where Y is the anticipated level of SA's, and X is the actual level of IA's (per 1,000 pregnancies). However, this pattern was not confirmed in other statistical groups, which is evidence of differences in the cross correlation between IA's and SA's.

Study of the consequences of preceding abortions in relation to the outcome of pregnancies showed that the risk of the principal groups of obstetric and perinatal pathology increases significantly in this case. For example when more than five IA's have occurred prior to a pregnancy, the risk of hemorrhage in the early period increases by more than 30 times, while the risk of impaired delivery increases by more than five times. Growth in failure to carry the fetus to term, intrauterine hypoxia and asphyxia during delivery and perinatal mortality is statistically significant in this case ($p < 0.01$).

Thus regional features have evolved in the Azerbaijan SSR in relation to the social and hygienic characteristics of abortions, which may become an object of control with the purpose of preventing obstetric and perinatal pathology.

References

1. Agayev, F. V., in "Syezd gigiyenistov i sanitarnykh vrachey Azerbaydzhana, 4-y: Materialy" [Congress of Hygienists and Public Health Physicians of Azerbaijan, 4th: Proceedings], Baku, 1981, pp 342-344.

2. Agayev, F. B. and Garayeva, S. G., "Puti profilaktiki materinskoy smertnosti v Azerbaydzhanskoy SSR: Metod. rekomendatsii" [Ways of Preventing Maternal Mortality in the Azerbaijan SSR: Methodological Recommendations], Baku, 1989.

3. "Zdravookhraneniye v SSSR" [Public Health in the USSR], Moscow, 1988.

4. Katkova, I. P. and Kravchenko, N. A., "Sotsialnoekonomicheskiye aspekty i planirovaniye semi" [Family Socioeconomic Aspects and Planning], Moscow, 1977.

5. Katkova, I. P. and Koshovskaya, T. V., SOV. ZDRAVOOKHR., No 9, 1989, pp 53-57.

6. Muchiyev, G. S. and Frolova, O. G., "Okhrana zdorovya ploda i novorozhdennogo v SSSR" [Protection of the Health of the Fetus and Infant in the USSR], Moscow, 1979.

7. Retkina, I. Ye., ZDRAVOOKHR. ROS. FEDERATSII, No 8, 1988, pp 16-19.

8. Usinskaya, I. V., ZDRAVOOKHR. ROS. FEDERATSII, No 8, 1988, pp 21-23.

9. Mahmood, T. A., Lim, B. H. and Lees, D. A. R., HLTH. BULL., Vol 46 No 6, 1988, pp 330-337.

10. Obel, E. B., ACTA OBSTET. GYNEC. SCAND., Vol 58, 1979, pp 485-490.

Medical, Demographic, Social and Hygienic Aspects of Infant Mortality and Factors Responsible for It

917C0570C Moscow SOVETSKOYE ZDRAVOOKHRANENIYE in Russian No 3, Mar 91 pp 34-38

[Article by doctors of medical sciences P. P. Petrov and D. Z. Borokhov, candidate of medical sciences M. K. Kulzhanov, and G. T. Kashafutdinova, Scientific Research Institute of Hygiene and Occupational Diseases of the Kazakh SSR Ministry of Health]

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[Text] Mortality indicators for children in the first year of their life have been adopted by WHO as control criteria to be used as guidelines in efforts to achieve a universally healthy society by the year 2000. In the opinion of experts, an infant mortality attaining 50 per 1,000 newborn infants is the limit at which it begins to have a retarding influence on the society's development [13]. In prerevolutionary Russia, infant mortality attained 268.6 cases per year per 1,000 births. During the years of Soviet rule, child mortality indicators decreased by more than a factor of 10 in the country, but beginning in the mid-1960s they began tending toward stabilization, and now they are holding at 25.4-25.5 cases per 1,000 births. As a result we are in one of the last places among economically developed countries of the world in infant mortality. Regional differences in the indicators evoke special alarm. While in the Baltic republics infant mortality is 11.6-16.0 cases, it is 46.2 in the Uzbek SSR, 46.7 in the Tajik SSR and 58.2 cases per 1,000 births in the Turkmen SSR [2,11].

Fundamental restructuring in the life of society, the course taken by the party toward solving many previously unsolved social problems, and the main directions in the development of public health and restructuring of USSR public health in the 12th Five-Year Plan and in the period to the year 2000 make reduction of infant mortality one of the priority problems. However, this is often viewed as a purely public health problem in specific-purpose and comprehensive health ["Zdorovye"] programs currently being written [1,5,6,8,10,14].

We attempted to make a socioeconomic assessment of the problem of infant mortality, and analyze the significance of the factors responsible for it.

The research was carried out in the Kazakh SSR, and it was based on materials from currently operating information systems of public health organs, and on the basis of government statistics for 1986-1987.

Infant mortality exhibits positive dynamics in Kazakhstan. In the last 10 years its level decreased by 25.3 percent to 29.0 cases per 1,000 newborn infants. Although infant mortality in rural areas was significantly higher than in the city (by 19.2 percent) throughout the entire period, the rate of its reduction was also higher (correspondingly 27.3 and 20.1 percent) [11].

The extent of the socioeconomic loss resulting from infant mortality was revealed on the basis of three of the republic's oblast centers—Dzhambul, Tselinograd and Chimkent, with a total population of over 1 million. Real and hypothetical tables of average life expectancy (ALE) were compiled for each city on the basis of data from currently operating information systems. In order to assess the influence of infant mortality on the basic economic and demographic indicators, two calculation variants were selected as a way to permit an alternative hypothesis—the case where infant mortality remains constant over time, and the case where its influence on the principal ALE parameters is totally excluded.

Calculations were carried out with a YeS computer using the specially written "Prioritet"[1] program making it possible to establish what influence the cause of death under investigation had upon the average life span of working-age individuals [3], on the extent of the population's participation in social production [4], and on the final results (the net coefficient) of the population's reproduction, in addition to determining its influence upon ALE [9].

The analysis showed that infant mortality has a significant influence on the principal economic and demographic indicators of the future development of the urban population. The mortality of children in their first year of life that has established itself in Dzhambul, Tselinograd and Chimkent will reduce the ALE of the urban population by 1.6-2.8 years, the number of persons living until they are of working age by 2.2-3.8 percent, the subsequent life span of each generation within the bounds of working age by 0.9-1.5 years, the predicted participation of the population in social production by 2.2-3.6 percent, and the end results (net coefficient) of the population's reproduction by 1.9-3.0 percent (see table).

Effect of Infant Mortality on the Principal Economic and Demographic Indicators of the Urban Population

Indicator	Dzhambul	Tselinograd	Chimkent
Mortality of children in their first year of life per 1,000 births	38.3	22.3	31.0
Number of years in the ALE of infants	69.7	70.1	68.6
Probable increase in indicators when influence of infant mortality on them is excluded			
Number of years in the ALE of infants	2.8	1.6	2.2
Percent living to the beginning of working age	3.8	2.2	3.1
Average number of years of subsequent life at working age	1.5	0.9	1.2
Effect of mortality on predicted participation of population in social production, %	3.6	2.2	2.8
Effect of mortality on end results of the population's reproduction, %	1.9	2.9	3.0

It should be noted that the predicted influence of infant mortality on economic and demographic indicators is significantly greater for the male than for the female population.

In the case where employment and labor productivity indicators remain constant over time, the predicted social and economic losses resulting from the evolved level of infant mortality will be, in cost terms, R41.9 million in Chimkent, R37.5 million in Dzhambul and R18.2 million in Tselinograd due to nonparticipation of infants dying at an age of up to one year in 1987. In other words one case of infant death in the republic causes a loss of R139,800 to the society.[2]

The causal structure of infant mortality in Kazakhstan is subject to significant regional variations. These differences are apparently not only the consequence of the actual frequency of particular pathological states but also to a certain degree they are the product of the interpretation of these states [12]. It should be noted, however, that as infant mortality decreases, the proportion of decedents who die in the perinatal period increases abruptly.

Despite variations in the total volume of the socioeconomic loss inflicted by infant mortality, pathological states arising in the perinatal period and respiratory diseases, which are responsible for 70-80 percent of all deaths, occupy the leading place universally. Next in line in the structure of the causes of death are congenital abnormalities (9.3-18.6 percent), followed by infectious diseases (up to 16 percent) and diseases of the digestive organs (up to 1.5 percent).

In the republic, infant mortality indicators vary within rather wide limits: from 22.8 to 53.3 cases per 1,000 newborn infants. This motivated us to use the methods of correlation analysis to determine the relative importance of individual factors affecting this phenomenon.

Infant mortality indicators differentiated with respect to the oblasts of Kazakhstan and similarly differentiated mortality indicators for children dying in the first year of life due to particular causes, health indicators of children, availability of medical care to them, and socioeconomic indicators of the population's standard of living were used in the analysis as the variational series. Correlation coefficients were computer-calculated according to the commonly used procedure [7].

Correlation analysis of regional features of the causes of infant mortality showed that deaths of children in the first year of life due to respiratory diseases ($r = 0.813$), intestinal infections ($r = 0.678$) and infectious diseases ($r = 0.476$) have the greatest effect on its level, while diseases of the perinatal period ($r = 0.143$) have less of an effect.

The magnitude of regional coefficients of infant mortality are correlated most closely with the principal socioeconomic indicators of the development of Kazakhstan's individual oblasts. It is inversely proportional to the local availability of children's preschool institutions to the child population (r = -0.631), to the availability of medicines (r = -0.611), to housing conditions (r = -0.568), to the volume of personal services (r = -0.510), to retail commodity turnover in state and cooperative trade (r = -0.466), and to the volume of foodstuffs sold by enterprises of state and cooperative trade (r = - 0.305).

Among indicators of the health of children in the first year of life, nutritional disorders (r = 0.552), the proportion of children who are ill frequently and over long periods of time (r = 0.499), ricketts morbidity (r = 0.455), and total morbidity of newborn infants (r = 0.312) occupy the leading place. The correlation between the frequency of unsuccessful pregnancy and infant mortality indicators is weak (r = 0.140).

The correlation between infant mortality and availability of medical care to the child population was the lowest. A negative correlation of moderate degree is observed between mortality of children in the first year of life and availability of pediatric beds to the child population (r = -0.441). The cross correlation between availability of pediatricians to the child population and the number of children per pediatric service section is weak (correspondingly r = -0.149 and r = - 0.068).

Thus the analysis showed that a significant number of factors responsible for regional variations in infant mortality are beyond the control of public health organs, which must be accounted for when drawing up the corresponding "Zdorovye" programs.

Conclusions

Despite a significant decrease, infant mortality continues to be one of the most important problems. It inflicts enormous social and economic losses on the society, reducing participation of each generation in social production by 2.2-3.6 percent; among factors responsible for regional features of infant mortality, the level of socioeconomic development of individual territories occupies a noticeable place. This requires an integrated approach to solving problems directed at reducing mortality of children in their first year of life.

Footnotes

1. Borokhov, D. Z., Petrov, P. P., Kulzhanov, M. K. et al., "Programma 'Prioritet,' prinyataya OFAP Minzdrava SSSR dlya otsenki na YeS EVM sotsialno-gigiyenicheskoy effektivnosti zadach, napravlennykh na uluchsheniye sostoyaniya zdorovya naseleniye" [The "Prioritet" Program Adopted by the USSR Ministry of Health OFAP for YeS Computer Assessment of the Social and Hygienic Effectiveness of Projects Directed at Improving Public Health], OFAP Minzdrava SSSR, 1989, pp 122; State Registration No 50890000913.

2. Calculations were carried out on the basis of data published in the collection "Narodnoye khozyaystvo Kazakhstana v 1987 godu" [Kazakhstan's National Economy in 1987], Alma-Ata, 1988, pp 368.

References

1. Albitskiy, V. Yu., SOV. ZDRAVOKHR., No 3, 1989, pp 31-34.

2. Baranov, A. A., SOV. ZDRAVOKHR., No 3, 1989, pp 3-6.

3. Bednyy, M. S., "Prodolzhitelnost zhizni" [Life Span], Moscow, 1969.

4. Borokhov, D. Z., VESTN. STATISTIKI, No 1, 1975, pp 30-34.

5. Baganov, I. N., Grebysheva, I. I., Kuznetsova, V. V. and Tsimlyakova, L. M., SOV. ZDRAVOOKHR., No 3, 1989, pp 7-11.

6. Ventskauskas, A. V. and Dreyerene, V. F., PEDIATRIYA, No 4, 1987, pp 8-10.

7. Ivanov, S. V., in "Statisticheskiye metody i vychislitelnaya tekhnika v sotsialno-gigiyenicheskikh issledovaniyakh" [Statistical Methods and Computer Technology in Social and Hygienic Research], Moscow, 1977, pp 122-164.

8. Katkova, I. P., Kravchenko, N. A. and Khusnutdinova, Z. A., SOV. ZDRAVOOKHR., No 3, 1989, pp 11-16.

9. Korchak-Chepurkovskiy, Yu. A., in "Sovetskaya demografiya za 70 let" [Seventy Years of Soviet Demography], Moscow, 1987, pp 263-280.

10. Lukyanova, Ye. M., PEDIATRIYA, No 1, 1987, pp 5-8.

11. "Naseleniye SSSR. 1987: (Statisticheskiy sbornik)" [The USSR Population. 1987: (Statistical Collection)], Moscow, 1988.

12. Nikonova, T. N. (Editor), "Pnevmoniya u detey rannego vozrasta" [Pneumonia in Young Children], Alma-Ata, 1984.

13. "Razrabotka kontrolnykh pokazateley dlya rukovodstva v rabote po dostizheniyu zdorovya dlya vsekh v 2000 g." [Development of Control Indicators as Guidelines in Efforts to Attain a Universally Healthy Society in the Year 2000], Geneva, 1982.

14. Terlitskiy, A. A., ZDRAVOOKHR. ROS. FEDERATSII, No 6, 1989, pp 12-15.

Effect of Chronic Internal Irradiation by Incorporated Radionuclides on Liver Function

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[Text] It has been shown by numerous experimental studies that irradiation by relatively large doses of radionuclides, especially hepatotropic radionuclides, leads to changes in liver morphology and function. Liver function in response to prolonged exposure to relatively small doses of incorporated radionuclides in the human body has hardly been studied.

From May 1986 through November 1989 we studied the concentration of radionuclides in liver tissue and their release with bile in persons located in areas subjected to radioactive contamination, as well as the effect of chronic internal irradiation upon liver function.

The following radionuclides were determined predominantly in liver tissue in 1986: lanthanum-140, tellurium-132, niodymium-147, barium-140, neptunium-239, zirconium-95, niobium-95, iodine-131, cerium-144, cerium-141, cesium-134 and cesium-137. In 1987-1989 we determined cerium-144, ruthenium-106, thorium-228, thorium-232, radium-226, zirconium-95, antimony-125, europium-154, cesium-134 and cesium-137. Typically, total radioactivity of liver tissue was 19-31 percent higher than that of blood in 1986, a total of 24-35 percent higher in 1987-1988, and 26-38 percent higher in 1989. In May-July 1986 we determined lanthanum-140 (as much as 60 percent of total activity), cerium-141 and cerium-144 (as much as 15 percent of total activity) in liver tissue; the specific concentration of cesium-134 and cesium-137 did not exceed 10-21 percent. In 1987-1989 the specific activity in liver tissue was 35-65 percent for cerium-144; 25-28 percent for radium-226, thorium-223 and thorium-232; and as much as 9-14 percent for cesium-137.

Moreover, ruthenium-103 was detected in the liver in the first 9-12 months (5-8 percent of total activity), whereas ruthenium-106 was detected later on (7-19 percent of total activity). The total activity of these radionuclides in liver tissue was 4.22-133 μCi/kg in May-June 1986, 0.25-25.6 μCi/kg in July-November 1986, 5.12-39.78 nCi/kg throughout 1987-1988, and 6.21-45 nCi/kg in 1989. The radionuclide content in liver tissue was determined during this period in 147 persons. All of the radionuclides we studied were released actively with bile into the lumen of the gastrointestinal tract. Their content in bile is shown in Table 1.

Table 1. Release of Radionuclides (in nCi/liter) With Bile in Various Periods After the Chernobyl Nuclear Power Plant Accident ($M + m$)

	Radionuclide Activity							
	Times of Analysis							
Radionuclide	May-Aug 1986	Sep-Dec 1986	Jan-Apr 1987	May-Sep 1987	Jul 1987-May 1988	Jul-Oct 1988	Jan-May 1989	Oct-Dec 1989
Iodine-131	15.4	2.1	0	0	0	0	0	0
Lanthanum-140	9866.4	124.5	91.2	0	0	0	0	0
Barium-140	1112.2	98.45	12.66	0	0	0	0	0
Tellurium-132	128.24	45.67	6.42	0	0	0	0	0
Neodymium-147	66.90	9.24	0	0	0	0	0	0
Neptunium-239	91.45	8.67	0	0	0	0	0	0
Ruthenium-103	67.56	45.62	22.14	11.67	10.55	9.12	1.14	0.25
Ruthenium-106	44.21	21.45	17.64	14.55	12.48	10.13	18.24	-19.74
Zirconium-95	56.42	31.27	25.42	21.12	11.71	9.24	0	0
Niobium-95	67.87	44.15	19.67	14.61	12.22	10.87	6.12	0
Cerium-141	67.24	31.24	22.15	11.45	8.21	2.01	0.12	0
Cerium-144	55.45	42.12	28.11	14.27	12.55	17.62	18.24	-17.45
Cesium-134	15.22	15.81	10.31	9.34	8.41	7.55	4.21	3.17
Cesium-137	16.24	12.42	11.24	10.87	11.22	8.45	9.21	5.24
Radium-226	0	0	6.45	5.87	4.24	3.67	4.68	5.12
Thorium-228	0	4.12	5.27	4.76	5.11	4.57	5.18	4.11
Thorium-232	0	3.18	4.26	3.87	3.27	4.62	4.29	3.89
Antimony-125	0	0	2.87	4.11	3.65	2.89	3.16	3.47
Europium-154	0	0	0	0	4.24	3.67	3.67	4.78

The total activity of radionuclides in bile was 2.44-25.67 μCi/liter in May-July 1986, 4.67-32.87 nCi/liter in September-December 1986, 24.67-65.74 nCi/liter in 1987-1988, and 2.98-72.56 nCi/liter in 1989. Simultaneous determination of the indicated radionuclides in pancreatic and gastric juice showed that no more than 1.5 percent of the radionuclides released into the lumen of the gastrointestinal tract with bile and with pancreatic and gastric juice was eliminated daily with feces, which is an indication of active reincorporation of radionuclides from the intestinal lumen.

These data indicate that both the body as a whole and the liver, the bile ducts, and the gastrointestinal tract were subjected to constant irradiation due to incorporated radionuclides. It is also obvious that besides hepatotropic radionuclides, there were various quantities of uniformly distributing and osteotropic radionuclides in liver tissue. Typically, neither iodine radioisotopes (in the initial periods) nor cesium radioisotopes (in the subsequent periods) played the dominant role in forming the internal radiation doses to which the liver and gastrointestinal tract were exposed for almost four years after the accident.

It seemed advisable to study liver function in persons subjected to constant internal irradiation by incorporated radionuclides. To do that, we studied the activity of AST, ALT, guanase, alkaline phosphatase, and sorbitol dehydrogenase and the content of total protein and protein fractions, prothrombin, bilirubin, fibrinogen, urea and creatinine in blood during 1986-1989. The liver's absorption-elimination function was assessed on the basis of data from the sulfobromophthalein sodium or uyevidin [transliteration] test, while hepatic circulation was assessed by tetrapolar rheohepatography. In addition, the liver was subjected to ultrasonic scanning with an Aloka echotomoscope (Japan), and the stomach and duodenum were subjected to endoscopic analysis by means of Olympus fibrogastroscopes (Japan).

A total of 1,415 persons were examined. Information for analysis was selected on 1,167 individuals who, according to thorough examinations, had been essentially healthy and had suffered no diseases of organs of the gastrointestinal tract prior to contact with radioactive materials. Table 2 provides data reflecting the frequency of appearance of various functional disorders of the liver in patients after they left the radioactive contamination zone.

Table 2. Frequency and Nature of Symptoms of Hepatic Functional Disorders in People (n = 1167) in Response to Chronic (2-3 week) Exposure to Radionuclides (data for the first [illegible] years after the accident at the Chernobyl Nuclear Power Plant)

Sign	Frequency of Detection, in %
Heavy feeling in right hypochondrium	69.6
Pain in liver area	6.7
Dyspeptic phenomena	45.5
Enlargement of liver	3.1
"Hydrophilic" liver tissue according to ultrasonic analysis	11.5
Elevated bilirubin	7.5
Elevated activity of:	
ALT	37.4
AST	28.2
Guanase	38.2
Alkaline phosphatase	18.1
sorbitol dehydrogenase	14.8
Reduced prothrombin content	12.7
Reduced total proteins	10.1
Reduced albumin level	17.7
Lengthening of uyevidin half-life	15.7
Reduction of relative hepatic clearance	15.9
Reduction of hepatic circulation	18.9
Thickening of gallbladder walls	18.6
Impairment of gallbladder contractile function	16.0
Erosive changes in gastric and duodenal mucosa	14.1

Thus, in the period immediately following departure of the subjects from the radioactive contamination zone, signs of impaired liver function developed: prothrombin- and protein-synthesizing, detoxifying, absorption-elimination signs. Elevated activity of ALT, AST and guanase in the blood of 28.2-38.2 percent of the patients indicates impairment of hepatocyte function. At the same time, impairment of the function of the gallbladder or thickening of its walls was observed in 18.6 percent of the patients, and erosive changes in the gastric and duodenal mucosa were observed in 14.1 percent. Ultrasonic scanning revealed liver enlargement in 3.1 percent of the patients and "hydrophilic" phenomena in liver and gallbladder tissue in 11.5 percent.

Systematic observations showed that clinical manifestations of impaired liver function disappeared in 998 (85.5 percent) of the 1,167 patients after two to six weeks as a result of treatment. However, elevated activity of ALT, AST and γ-glutamyl transferase (GGT) persisted in 169 (14.5 percent) of the individuals for six to eight months, exceeding the norm by two to three times in 97 (8.3 percent). A parallel was revealed between the radionuclide levels in bile, pancreatic and gastric juice, and blood, on one hand, and the degree of impairment of the activity of hepatospecific enzymes, on the other. An elevated prothrombin index was established in 124 (10.6 percent) of the individuals, and a reduced index was noted in 23 (2.0 percent). During the first 1.5 years after the first contact with radionuclides, a 5-11 percent decrease in total proteins was observed in the blood of 217 persons, and an 8-15 percent decrease in albumin was observed in 279. Changes in the proteinogram characterizing a relative increase in the content of alpha-1 and alpha-2 proteins by 7-15 percent were revealed in the data for these patients.

Over the long term (two to four years after the accident at the Chernobyl Nuclear Power Plant), development of acute or chronic cholecystitis, hepatitis and pancreatitis was noted in 280 (23.9 percent) of the patients. Morbidity and the incidence of these diseases in the group of persons subjected to chronic internal irradiation were 2-3.1 times higher than among unexposed individuals during the time of observation. A 36-41 percent increase in destructive forms of disease, a more serious course, and greater severity of the endotoxic syndrome were revealed in the structure of acute cholecystitis and acute pancreatitis. Typically, in acute surgical diseases, liver and kidney function worsened considerably as early as in the first two to three days, with acute hepatorenal insufficiency developing twice as often. Thrombohemorrhagic complications developed 36.6 percent more frequently among these patients. The course of treatment of irradiated patients was 1.4 times longer and rehabilitation time was 1.7 times longer than among unexposed patients.

This research showed that prolonged exposure to incorporated radionuclides causes development of functional disorders in the liver in 20-30 percent of patients, with subsequent development of acute or chronic disease in the liver, gallbladder, or pancreas. Soon after irradiation, the laboratory signs of functional disorders of the liver (on the basis of data from analyzing the activity of ALT, AST and GGT and from the uyevidin test) are observed in 20-45 percent of the patients. A parallel was revealed between the degree of impairment of liver function and the level of radionuclides in the body.

Employment of various hemo- and enterosorption procedures that use modified sorbents, in combination with physical and chemical methods and accelerated elimination of radionuclides, promoted faster recovery of liver function in persons subjected to internal irradiation, plus a more favorable course in acute diseases.

Conclusions

1. Both hepatotropic and uniformly distributing radionuclides are detected in liver tissue, bile, and pancreatic and gastric juice of people who had worked in radioactive contamination zone, with hepatotropic radionuclides dominating. The nature of their elimination from the body changes when chronic exposure occurs.

2. Prolonged action of incorporated radionuclides leads to development of transitory functional disorders in the liver of 20-45 percent of patients, and acute or chronic diseases of the liver, gallbladder or pancreas in 20-30 percent. A parallel was revealed between the levels of incorporated radionuclides in the human body and in liver tissue, on one hand, and the degree of impairment of liver function, on the other.

3. Accelerated elimination of radionuclides from the body is a means of preventing functional and organic injury to the liver, gallbladder and pancreas.

Problems of Medical Radiobiology

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[Text] This report examines two aspects of medical radiobiology:

(1) scientific substantiation of the therapeutic use of ionizing radiation, above all, improvement of radiation methods for the treatment of cancer;

(2) radiobiological assessments of the consequences of radiation loads on the population resulting from diagnostic use of ionizing radiation and prolonged exposure to low levels of radiation stemming from the accident at the Chernobyl Nuclear Electric Power Plant.

The authors felt it necessary to include in the report, data obtained in the interval between the previous and present all-union congresses of the society of roentgenologists and radiologists.

1. Radiobiology and Radiation Treatment of Tumors

During the indicated period, work on radiomodifiers was the most extensive and successful work in research directed at creating new radiation treatment techniques in our country. Hyperthermy may be ranked first among them. We take pleasure in noting that all experimental and clinical studies conducted in this field make use of Soviet-made instrumentation. The fact that half of the 20,000 patients who have received hyperthermic treatment throughout the world thus far received it in institutions in our country is evidence of the relative role played by Soviet specialists.

Radiobiological research (in the field of oncology, radiobiologists are the ones who are primarily engaged in hyperthermia) have shown that heating tumors to 41-43°C intensifies destruction of the radioresistant part of a population of tumor cells—for example, cells in a state of hypoxia. The selectivity of the action of high temperature is associated in this case not with higher heat sensitivity of tumor cells as such, but with their imperfect blood supply, which is unable to support adequate heat removal, as a result of which tumors undergo selective overheating. It turns out that increasing the temperature of tumor tissue just 2-4°C above normal causes a substantial number of neoplastic cells to die.

Polyradiomodification methods were developed in a number of institutions during these years. The methods entail simultaneous and/or successive use of several agents

and radiation in a specially selected temporal combination, with hyperthermia as the central component. As in the case of hyperthermia, the selectivity of hyperglycemia is associated with the existence of an imbalance in the growth of parenchyma and development of the capillary network in tumors, such that as a result of insufficient oxygenation the glycolytic pathway of energy production becomes dominant, causing acidification of the tumor as a result of addition of glucose. In turn, reduction of pH raises the heat sensitivity of the cells, inhibits repair of radiation injuries, and, in altering the rheological properties of erythrocytes, promotes suppression of circulation—that is, reduction of heat removal.

Comparative research on animals with transplanted tumors showed that the therapeutic advantage created by combining hyperglycemia and hyperthermia may attain a factor of three (S. V. Kozin et al., S. P. Yarmonenko et al.)—that is, a value exceeding the indicators cited in works on experimental radiation therapy.

We note in passing that development of the methods of impairing tumor circulation—for example, by means of selective damage to the capillary network's endothelial cells—holds great promise, and it is now becoming one of the central objectives in the programs of leading foreign institutions.

We present data from the Scientific Research Institute of Oncology and Medical Radiology of the Belorussian SSR Ministry of Health as examples of the use of the modifiers examined above. The treatment of 230 patients with stage II-IV dermal melanomas (the extent of the process in 186 patients was within T3b-4N0M0) entailed 10-13 daily thermal radiotherapy sessions (42-43°C for 2 hours, followed by irradiation at a dose of 4-5 Gy, for a total dose of 50-52 Gy), after which surgery was performed. When the wound healed, the patients were irradiated under the usual fractional radiation conditions for a total dose of 20-30 Gy. The five year survival rate of patients was 76.9 + 4.7 percent, whereas the survival rate in a control group of 36 patients, who were not subjected to hyperthermia, was 52.8 + 5.8 percent. It was established later on in an investigation of the sequence of using hyperthermia and irradiation that it is preferable to do heat treatments after irradiation.

When 40 patients with soft-tissue sarcomas were subjected to combined treatment, the combination of irradiation and hyperthermia resulted in a five year cure for 54.6 + 7.9 percent of the patients, and a combination of hyperthermia and chemotherapy resulted in a five year cure of 63.6 + 6.3 percent (43 patients in the group). At the same time, in the absence of hyperthermia (33 patients), that figure was only 38.3 + 8.8 percent. It was found in a random study on 51 patients with cancer of the urinary bladder that combining intrabladder hyperthermia with preoperational radiation therapy resulted in a three year survival of 94.1 + 4.1 percent of patients, whereas the survival rate was 66.6 + 7.2 percent for 51 patients of the control group (treatment without hyperthermia). Recidivism over an observation period of three years was 20.6 + 7.5 percent and 41.4 + 6.9 percent, respectively.

The effectiveness of hyperglycemia (22-33 mM in blood serum) as an adjuvant of preoperational radiation therapy was evaluated in a random study on 379 patients with stage I-III large-cell [nemelkokletochnyy] lung cancer. Establishment of hyperglycemia prior to fractions I, III and IV out of five irradiation fractions of 4 Gy each, up to a total dose of 20 Gy, or immediately after applying these fractions, resulted in five year patient survival rates of 50.6 + 10.9 percent and 51.5 + 8.2 percent, respectively; while in the control group it was 34.9 + 4.8 percent. The Second All-Union "Hyperthermia in Oncology" Symposium, held in late May 1990 in Minsk, in which leading foreign scientists participated, graphically demonstrated the great possibilities of using these agents in radiation treatment of tumors.

An alternative means of widening the therapeutic interval is selective protection of normal tissues at a corresponding level of protection by increasing the radiation dose and, consequently, intensifying the injury to tumors. To date, the USSR has accumulated experience in treating around 1,000 patients by using general hypoxia as a radioprotective agent, with the hypoxia created by inhalation of a gas mixture containing 10 percent, 9 percent and even 8 percent oxygen at the moment of exposure to radiation. Short-term hypoxia, which has no side effects, makes it possible to increase the applied dose by 20-30 percent. Two examples are presented for the purposes of illustration.

1. A procedure of intensive preoperational hypoxic radiotherapy for a stomach cancer was developed at the Dnepropetrovsk Oblast Oncological Dispensary, with the participation of All-Union Scientific Center for Oncology specialists (radiobiologists, x-ray therapists, surgeons). The patients were exposed to a dose of 4 Gy three times a week with 14 x 16 cm to 16 x 20 cm fields. These fields included zones which, when subjected to radiation injury, elicit unrestrainable vomiting and other serious reactions. When irradiation was performed under hypoxic conditions (8 percent oxygen), the total dose could be raised to 36-44 Gy in 83 percent of the patients; when ordinary atmospheric air was inhaled, only 20 percent of the patients could withstand such a dose. Extremely serious reactions that could not be relieved by drugs were noted in 19 percent of the patients treated under hypoxic conditions, but in 63 percent of patients who inhaled atmospheric air and were irradiated with an even smaller dose (28-32 Gy). Morphological and cytological analysis of surgical preparations did not reveal any attenuation in radioactive destruction of tumors. Thus, it may be assumed that the protection provided by the hypoxic mixture corresponded under these conditions to an FID [not further expanded] of 1.4.

The most important result of these studies was the possibility they presented for widening the group of patients selected for combined treatment, which helped increase the five year survival rate to 57 percent, as compared to 30 percent in the group of patients treated only by surgical means.

2. The Institute of Clinical and Experimental Oncology (Brno, Czechoslovakia) conducted a random study of the possibility of using a mixture containing 8 percent oxygen to raise the effectiveness of combined radiation therapy for

cervical cancer (T. Tachev). Hypoxic radiotherapy was carried out in the stage of remote gamma-irradiation (the irradiation zone was expanded as necessary to include involved lymph nodes); in addition, the dose was increased by 40 percent (from 40 to 56 Gy), owing to which it attained 96 Gy at point A and 75 Gy at point B.

Communicating the direct results of treatment, the authors note good tolerance of "radical" hypoxia (8-8.5 percent oxygen) by absolutely all patients (a total of 1,000 treatments were carried out), making it possible not only to avert serious complications, but also, despite a substantial increase in the dose, to halve the frequency of mild radiation reactions of the rectal mucosa, as well as to completely remove the symptoms of intestinal irritation observed in patients of the control group, who were exposed to lower doses.

Substantial attenuation of radiation reactions by mucous membranes and improvement of long-term indicators were achieved in a random study as a result of the use of hypoxia in radiation treatment of laryngeal cancer (Yu. S. Mardynskiy).

Use of general hypoxia when irradiating retroperitoneal tumors and pancreatic neoplasms (G. V. Goldobenko) has become a routine method of treatment at the USSR Academy of Medical Sciences' All-Union Scientific Center for Oncology.

Interest in more "aggressive" methods of tumor treatment, including application of the largest possible radiation doses, has been noted throughout the entire world in recent years.

The experience of the Scientific Research Institute of Oncology and Medical Radiology of the BSSR Ministry of Health shows that raising the dose of preoperative irradiation when treating breast, lung and stomach cancer to levels isoequivalent to carcinolytic doses (55-70 Gy, based on gross fractionation) improves the near-term and long-term results.

Combining radiation therapy conducted in doses typical of a radical treatment program and radical surgery in the treatment of more than 1,000 patients with such cancers resulted in a five year survival rate that was better than the rates with purely surgical or traditional combined treatment by a factor of 1.3-1.6. For example, the five year survival of patients with stage III breast cancer increased to 59 + 4 percent from 46 + 3 percent, while that of patients with stage IIIb cancer increased to 58 + 4 percent from 35.3 + 3 percent. Similar treatment tactics applied to patients with epidermoid lung cancer increased five year survival to 45 + 3 percent from 32 + 4 percent.

Besides positive work results in these years, mention should also be made of major shortcomings in our programs in comparison with the results of foreign research. First of all, little basic research on clinical radiobiology is being conducted in our country. There are few laboratories developing new radiation treatment systems in oncological and radiological institutions, and such laboratories are even decreasing. Experimental developments undergo clinical testing much more slowly than they should. The percentage of random research based on a number of patients sufficient for statistically meaningful conclusions is extremely low, and follow-up on the fate of patients after their treatment is poorly organized. While research is highly centralized on paper, the efforts of different institutes working under the same program are not united.

In the conversion to a competitive system of financing research projects, it would be advisable to allocate small but special funds to pay for clinical testing of procedures developed by experimental subdivisions of our institutions, and to reward a doctor for every patient treated in an experimental program. In any case, the authors believe it fully justified to develop financial means of hastening evaluation of the results of experimental research in the clinic.

2. Radiobiological Evaluation of the Significance of Radiation Loads Upon the Population

In the literature available to the lay reader and even specialists, it is hard to find dependable and exhaustive data on the dose loads experienced by the USSR population from the principal radiation sources. At the same time, such information is needed by radiobiologists, physicians and other specialists having the need to determine the consequences of radiation exposure. Let us begin with the loads the population of our country received prior to the accident at the Chernobyl Nuclear Electric Power Plant. The average individual radiation doses determined by associates of the Biophysics Institute of the USSR Ministry of Health and some data published earlier are presented in Table 1.

Table 1. Average Individual Doses of Irradiation Received by the USSR Population in 1985, millirem/year (10^{-5} Sv/year)

	Doses to Individual Organs			Effective Equivalent Dose
Radiation Source	Red Bone Marrow	Lungs	Gonads	
Natural				
External cosmic radiation	32	32	32	32
External γ-radiation of natural nuclides in the Earth's crust	30	30	30	30
				(20-100)**
Internal irradiation due to ^{40}K in food	20	20	20	20
				(10-40)**

Table 1. Average Individual Doses of Irradiation Received by the USSR Population in 1985, millirem/year (10^{-5} Sv/year) (Continued)

	Doses to Individual Organs			Effective Equivalent Dose
Radiation Source	Red Bone Marrow	Lungs	Gonads	
Internal irradiation due to ^{226}Ra, ^{14} and tritium in food, water, air	10	4	4	8
	(100) *			
Industrially intensified background of natural radionuclides				
^{222}Rn and its daughter products on premises	7	1,200	5.0	140
		(100-33,000) **		(12-4,000) *
Nuclides in construction materials	10	10	10	10
Radionuclides in fertilizers	0.1	0.1	0.05	0.02
	(0.4) *			
Radionuclides in the volatile zone from coal-burning power plants	0.1	1.4	0.1	0.25
	(3) *			
Artificial:				
X-ray diagnosis	160	350	35	140
				0-15,000) **
Global ^{137}Cs and ^{90}Sr fallout	4.0	1.5	1.5	2.2
Nuclear power plants (with total output of 20 GW (electrical)***	0.035	0.025	0.015	0.2
Atomic industry enterprises***	0.03	0.03	0.01	0.15
All principal sources taken together	400	1,640	270	360
	(550) *			(100-20,000) **

*On endosteal cells

**Numbers in parentheses are minimum and maximum doses for segment of the population

***Not counting employee dose (averaging 500 millirems/year).

The following conclusions from the materials in Table 1 would best be singled out:

—Three sources make the main contribution to the population's dose: the natural background, radon in buildings and x-ray diagnosis;

—Irradiation of individual population groups differs primarily depending of the concentration of radon in dwellings and on the frequency and form of x-ray diagnostic analyses.

—The range of the average annual individual doses varies from 0.1 to 20 rem/year for different population groups. The number of residents for whom the effective equivalent exposure dose in dwellings attains 1 rem/year or more has not yet been established by means of direct determinations, but indirect data allow us to estimate it at around 1 million. It is entirely probable that we are on the verge of realizing that there is a radon counterpart of Chernobyl in the country that significantly exceeds Chernobyl in its radiological consequences. The role of other radiation sources in determining the average dose and its fluctuations is significantly lower. Among them, mention should be made of the dose rate of natural radionuclides in soil and in underlying rock (the so-called radiation background). It is usually 10-20 μR/hr, but it may vary from 4-8 μR/hr (in soil containing little radium, uranium, thorium or potassium) to 100 μR/hr or more, for example in the vicinity of the central granitic massif in France, on the monazite sands of the state of Kerala in India, and on Kalinin Square in Kiev, the fountains of which are surrounded by large amounts of granite rich in natural radionuclides.

The radiation situation in the country, and especially in southeastern Belorussia, the northern Ukraine and the western RSFSR, changed considerably as a result of the accident at the Chernobyl Nuclear Electric Power Plant. Owing to the spread of fallout practically over the entire territory of the USSR, and as a result of imports of foodstuffs from contaminated regions, the average individual annual dose rates produced by a total (external and

internal) irradiation in the USSR population as a whole increased in 1986-1987 by an average of 10 millirem/yr, and in 1988-1989 by 5 millirem/yr—that is, by 1-3 percent.

Detailed data characterizing the total exposure dose and the amount of radiation received by the thyroids of the population of contaminated regions of Ukraine, Belorussia and the RSFSR are cited by L. A. Ilin *et al.* in the journal MEDITSINSKAYA RADIOLOGIYA, No 11, 1989.

Table 2 provides an assessment of the loads experienced by population groups subjected to the most substantial irradiation. The assessments were arrived at by generalizing data published in the press and available in the Biophysics Institute of the USSR Ministry of Health. However, there is no information on the professionals who took part in the effort to control the accident in the first few hours and days at the nuclear power plant itself and in its industrial environs, inasmuch as this paper examines exposure of the population as a whole. Moreover, the contribution of the dose received by professionals compared to the overall dose received by the country's population as a result of the accident at the Chernobyl Nuclear Electric Power Plant is small, despite the high individual doses of irradiation.

Table 2. Average Whole-Body Individual Doses of External and Internal Irradiation Received by Different Population Groups of Belorussia, Ukraine and RSFSR, Over 1986-1989 on Contaminated Territory

		Doses, rem, cSv	
Contingent	Contingent Size	First Year (1986/87)	1986-1989
Accident cleanup workers:			
First year	25,000	15 (up to 50-70)	-
1986-1989	500,000	-	10
Evacuees:			
From Pripyat	45,000	1.5 (maximum of 12)	3.0
From villages within 30-km radius	70,000	3 (maximum up to 50)	5.0
Population in controlled zones, with radioactive cesium contamination densities of, Ci/km^2:			
>15	270,000	3	6.0
>5	500,000	1.5	3.5
>2.5	2,400,000	0.3-1.0*	1.0*

*In actual conditions, substantial deviations from average values are observed for this category of the population (and to a lesser degree for other categories) owing to internal exposure dose having their origin in peculiarities of the soil and the soil's capability for binding and fixing cesium. For example, there are villages in Lelchitskiy Rayon, Brest Oblast, in which the internal irradiation dose accumulated over four years as a result of elevated migration of cesium through food chain approaches 1.5-2 rem, whereas in Gomel, where the contamination density is the same, the dose of internal and external irradiation was only 0.5 rem in 1986-1989 and less than 0.1 rem in 1989.

Commenting on Table 2, we would like to turn our attention to the fact that the individuals exposed to the maximum doses were primarily the accident cleanup workers who worked in the first months after the accident, when dosimetric control and observance of radiation safety rules were considerably less complete and effective than later on.

In that connection, the figures given in this paper for the actual doses experienced by accident cleanup workers are more qualitative or semiquantitative. Inasmuch as there were practically no cases of radiation sickness of even mild form among accident cleanup workers, and subsequent immunological research did not reveal a correlation between the immune status of the accident cleanup workers working in the "dirtiest" areas and the recorded or calculated exposure dose, we can conclude that even for the category of people exposed to high doses, the dose did not exceed 50-75 rem and was, on the average, around 20 percent of that value.

According to data of the Institute of Medical Radiology of the USSR Academy of Medical Sciences, of the 86,447 persons for whom dosimetric data were available, 77 percent received a dose of 5-25 rem, while 15 percent received less than 5 rem. The next group after accident cleanup workers that received the greatest amount of radiation consisted of the several dozen residents of a number of small villages within the 30 km zone or near it who were evacuated several days after the inhabitants of the city of Pripyat, and who managed to receive a dose close to 50 rem prior to their departure. As a result of the implemented measures, the actual dose loads decreased dramatically. However, as early as in 1987, a total of 38 persons were identified in the BSSR who deliberately ignored recommendations and prohibitions; their internal exposure dose resulting from consumption of milk from their cows, as well as mushrooms, exceeded 5 rem per year, and in one of the identified cases the dose reached 38 rem. However, in more than 95 percent of the population of contaminated regions, the interim (emergency) standards of radiation safety (10 rem in the first year, 3 rem in the second, 2.5 rem in the third, and 2 rem in the fourth year) were not exceeded, and measures adopted by the USSR Ministry of Health and the Agroindustrial Committee made it possible to reduce the actual exposure levels to dozens of times less than what they could have been. For example, the total dose of total irradiation (internal and external) for residents of the zone of strict surveillance in the BSSR was 0.560-0.760 rem in 1989; of that amount, no more than 0.250 rem was received in terms of irradiation from cesium ingested with food; the rest was due to external irradiation. These data are based on the

results of many thousands of analyses of foodstuffs and more than 150,000 measurements of the radioactive cesium levels in the bodies of residents by means of special Soviet and imported radiation counters intended for human use.

Considerably greater dose loads were received by thyroid glands, primarily the result of the intake of ^{131}I with dairy products and table greens in the first few days and weeks in locales where preventive iodine treatment was not conducted promptly or with sufficient completeness and where other protective measures were not implemented (importing clean milk and clean feed for farm animals). For example, according to data of the All-Union Scientific Center for Radiation Medicine of the USSR Academy of Medical Sciences (Kiev), more than 5,000 children in Ukraine received a dose that was above the standard dose (which was 30 rem), and of them, several dozen received as much as 1,500 rem.

What is the significance and what are the possible consequences of the population's exposure as a result of that accident? To answer that, it would be best to recall the basic effects of exposure to different doses, as generalized in Table 3.

Table 3. Basic Effects of Total Exposure in Dose-Effect Terms. Generalized Data From World Literature, Including Observations of the Consequences of the Accident in 1957 in the Southeastern Urals

Dose, rem (cSv)	Effects
More than 350 at one time	Acute radiation sickness (ARS), death
Greater than 75 and up to 350 at one time	ARS, temporary changes in blood cellular composition and immunity, a real (identifiable) risk of embryotoxic effects (microcephaly), genetic effects, and carcinogenic effects
Less than 75, but more than 25 at one time	Transitory changes in blood cellular composition, and other effects indicated above except for ARS—less pronounced, with a lesser risk of development of remote consequences, which in a number of cases are not detectable
Prolonged, more than 50 rem annually	Manifestations of chronic radiation sickness, reduction of nonspecific resistance, cataracts, remote probabilistic effects (with a probability of up to 500 cases of cancer per collective dose of 1 million man-rem)
Prolonged, less than 50 rem a year, but more than 15	Absence of any specific health disorders, reactions such as irritation, adaptation, maintenance of the risk of remote probabilistic effects, reduction of the function of generative organs, growth of the risk of cancer by 15%
At one time up to 15 rem, and prolonged—less than 5 rem annually (less than 50 rem total over a number of years)	Absence of effects, including remote probabilistic ones (the risk of the latter persists, but at levels of 0-5%, and they are not identifiable against a background of spontaneous morbidity)

Table 3 is presented to make it easier to assess the significance of existing dose loads upon the population of the USSR as a whole (see Table 1) and the population of territories contaminated by the accident at the Chernobyl Nuclear Electric Power Plant (see Table 2). The materials of Table 3 show that, in accordance with the notion that the carcinogenic action of radiation is independent of any threshold, we can expect a certain number of additional cases of cancer with a lethal outcome, as well as genetic disorders. The computations associated with such consequences are presented most completely in the previously cited article by L. A. Ilin *et al.*

Our tentative generalized data for different population groups are given in Table 4. In calculating the risk, we assumed that a collective dose of 1 million man-rem can cause 700 additional deaths from cancer, and not the 25 suggested in ICRP [International Commission on Radiological Protection] publication No 26. This increase in the assessed risk seems justified in light of the 1985 reexamination of doses of irradiation received by residents of Hiroshima and Nagasaki, which showed that the actual doses were below those previously used in the calculations, and in light of fuller consideration of the long-term consequences of the atomic bombing and the use of a model of relative risk. Nor do we decrease the risk by a factor of 2-5 as suggested by the United Nations SCEAR [Scientific Committee on the Effects of Atomic Radiation] for cases of protracted exposure (as in a reactor accident) in comparison with short-term exposure (as in explosion of an atomic charge). All of this permits us to arrive at figures characterizing the uppermost level of possible risk.

Table 4. Possible (Tentative) Consequences of Exposure of the USSR Population to the Total Dose Received in 1986-1989 (Long-Term Effects) and in the Forthcoming 70 Years (Up to 2060)

Group	Collective Dose, man-rem	Number of Possible Lethal Cases of Cancer	
		Additional, caused by irradiation	Spontaneous, due to various causes
Accident cleanup workers			
500,000—all who worked in the zone	5,000,000	0-2,000	71,400 ± 23,000
Including 25,000 exposed to the greatest amount of irradiation in 1986	375,000	0-150	3,570 ± 1,100

Table 4. Possible (Tentative) Consequences of Exposure of the USSR Population to the Total Dose Received in 1986-1989 (Long-Term Effects) and in the Forthcoming 70 Years (Up to 2060) (Continued)

Group	Collective Dose, man-rem	Number of Possible Lethal Cases of Cancer	
		Additional, caused by irradiation	Spontaneous, due to various causes
Evacuees:			
From Pripyat	135,000	0-68	6,400 + 2,200
From villages in the 30-kilometer zone	350,000	0-175	10,000 + 3,300
Population of controlled zones; level of ^{137}Cs contamination, Ci/cm^2:			
>15	1,620,000	0-810	38,600 + 12,500
>5	1,750,000	0-875	71,400 + 23,000
>2.5	1,400,000	0-700	200,000 + 70,000

Note: Several dozen lethal thyroid cancer cases should also be expected in all the groups.

A comparison of the dose-effect dependence data (see Table 2) and the actual dose loads experienced by the population (see tables 1 and 3) does not provide the grounds for expecting development of exposure-related illnesses and health disorders diagnosable in the clinic or in the laboratory among any population groups of the country, including the population of territories contaminated by the accident at the Chernobyl Nuclear Electric Power Plant. The accumulated radiation doses and the dose rate for the last year (0.56-0.76 rem for the year in 1989) are considerably below values which authoritative international organizations (SCEAR, ICRP) feel are capable of causing any kind of direct negative changes in health. Growth in morbidity indicators for most nosological forms, recorded everywhere on contaminated territories, obviously reflects improvements in identifying disease and not real growth of morbidity. There remains, however, the threat of random effects of radiation, manifesting themselves in somatic (cancer) and sex (hereditary diseases) cells. The level of risk for these diseases, however, is such that the extra number of cancer cases and especially hereditary defects would hardly be noticed against the background of spontaneous morbidity, even with very sophisticated record-keeping (currently nonexistent). It is highly probable that thyroid tumors will be identified later on as a consequence of the Chernobyl disaster.

Even if we were to accept the clearly overstated assessment of risk, it would seem that these materials would not raise any doubts as to the absence of detectable signs of radiation injury, were it not for the unending flow of alarming and terrifying reports of the health of people residing in "stricken" ("contaminated") or, more accurately, polluted territories.

The question, naturally, is this: How do we reconcile these facts? For specialists in radiation medicine, the answer is clear.

Our society is currently going through a "second Chernobyl"—considerably more dangerous to health than was believed earlier in the assessments of only the possible consequences of irradiation. We are referring to the "psychic Chernobyl," the epidemic of radiation fear that has stricken enormous masses of people. We are not going to go into the causes of this phenomenon here. We note, however, that the population itself is not to blame for this and does, in fact, require assistance. Among the "culprits" we can name our flawed system, which in the first stage provided false, excessively optimistic information and kept the real information secret even from specialists, which elicited deserved mistrust in the authorities, science and medicine. It is with even greater distress that we note the still-persisting, extremely low competency of medical workers, and even of a sizable part of radiobiologists, in matters of radiation medicine, radiation hygiene and the effects of low-level doses.

There is a tendency today for the mass media and for some doctors locally to associate practically all illnesses of the population with the action of radiation, including, for example, those caused by extremely unsatisfactory diet and social problems. As was noted above, better detectability of disease is interpreted in this case as higher morbidity. This assessment of the real situation stems in particular from a report written by a team of specialists from the USSR Ministry of Health that conducted an examination in Gomel in May 1990.

Often, isolated incidents—for example, the births of abnormal calves and of children with congenital defects—are interpreted as a natural result of exposure to radiation, which is a common mistake. Nonetheless, it disturbs millions of people. Note that when a number of reports concerning abnormalities among farm animals were carefully checked out by specialists of the State Agroindustrial Committee, a rise in abnormalities among these animals was not confirmed. In a number of cases, a rise in frequency of actually observed abnormalities turned out to be associated with inbreeding and with the action of mutagenic factors of a nonradioactive nature.

Nor has a substantial increase in the frequency of defects, typically associated with the effects of radiation, been identified in the population of contaminated territories.

Here are a few examples from the avalanche of mindless, sensationalistic reports that appeared, unfortunately, with the help of medical personnel. We know that a lengthy latent period is typical of radiation-induced malignant neoplasms

(4-5 years for leukoses and 10-20 or more years for solid tumors). In the meantime, a case of leukosis documented in a woman just one year after the accident (in 1987) was associated with her exposure to radiation while bathing "contaminated" children; there was also the young boy with chronic leukosis who was sent to the United States for treatment in connection with "overexposure in the first days of the accident." The death of a cameraman from a major case of cancer in 1987 was associated with radiation, even though the disease could not have developed so quickly. One of us heard from the lips of an authoritative specialist, whose name we find it uncomfortable to even mention, a tall tale concerning the simultaneous death of five "shearers of contaminated sheep," supposedly the result of cancer of the larynx in 1987. There are many reports of nosebleeds and fainting spells among children, and about their poor health; but they are all subjective and anecdotal, they lack epidemiologically correct quantitative assessments, they lack the required comparison with an adequate control, and they disregard other factors—in particular, poor nutrition and the consequences of keeping children indoors without exercise for days at a time, and so on. One of Moscow's central institutes told a number of Gomel's residents that according to chromosomal aberrations found in them, they had received a radiation dose of 40-70 rem. In reality, however, the total dose of external and internal radiation in Gomel—where the intensity of contamination of the city's territory by radioactive cesium varies within 1.7-2.3 Ci/km^2—was only 0.5 rem in four years (1986-1990), which is easily verified dosimetrically.

We do not know of a single case in which scientifically substantiated data definitely indicates a worsening of the health of children or adults as a result of the effects of radiation.

This premise, which is valid in relation to accidental total irradiation by gamma radiation, could obviously be extrapolated, though with less certainty, to the effects of irradiation of the thyroid gland, despite the truly large doses received by many thousands of people. For 1988-1990, there are reports of an increase in the frequency of hypertrophy of the thyroid gland—the initial stage of goiter (the contaminated territories are endemic in relation to goiter)—by a factor of approximately 1.5, and of hypotrophy by 40 percent. Despite the fact that the thyroid disorders are quite real, the cited data, or more accurately the suggestions that they are radiation-associated, nonetheless raise doubts, if we consider that the population is now being examined much more completely, using ultrasonic diagnostic methods, which were unavailable prior to 1986. Moreover, it would have been more likely to expect dominance of hypotrophic rather than hypertrophic reactions. Cases of autoimmune thyroiditis have also been identified, although it remains unclear as to whether their frequency exceeds the level prior to the accident. Nonetheless, thyroid tests should be continued, so that possible appearance of hypofunction or tumors, for which substitution therapy or surgery would be indicated, could be established as soon as possible.

In this situation of unchecked emotions and of careless and irresponsible statements, the role of reliable, clearly verifiable indicators of the health of the population, such as early child mortality, is increasing. Statistics show that early child mortality did not increase in the population of contaminated regions in 1986-1989, and that it is at a level similar to that for Western European countries. In the meantime, early child mortality is two to five times higher in the ecologically unfavorable regions of Siberia, the Urals, Ukraine and Central Asia (and not a result of radiation).

Thus, an analysis of four years of materials on the dose loads experienced by the population and on its health as a result of the accident at the Chernobyl Nuclear Electric Power Plant does not contradict the data of world science, and it does not provide any grounds for the "revolution," claimed by the mass media, in radiation medicine, oncology and radiobiology in regard to ideas about the effects of small doses. Nonetheless, it would also be wrong to understate the consequences of the Chernobyl accident in relation to the health and welfare of the population of contaminated territories and of the entire country, as regards the consequences of persistent fear and depression and as regards suggestions that residents would be doomed if they continued to live in these regions. In this situation, we can understand the government's decisions to resettle enormous masses of the population. However, everything possible should be done to keep fear and depression from being carried by the evacuees to new places of residence, because otherwise the anticipated positive impact of this expensive and traumatic measure will not be achieved.

When we evaluate the possible consequences of the accident in relation to the country's whole population, we should primarily consider not the direct effect of additional total exposure to 5-10 millirem annually, but the social result of diverting so many billions of rubles, the absence of which will have an effect on the supply of medicines and on public health as a whole and will delay adoption of measures to improve the situation in zones of ecological disaster, housing construction and so on. Millions of people are living in regions with no potential danger, but a real and present ecological danger that is taking the lives of our fellow citizens. Consider, for example, the industrial centers of the Urals and Siberia, and the rural areas of Central Asia, where morbidity and child mortality are much higher than in regions that suffered from the Chernobyl accident. It is completely clear that money should be spent in such a way as to save a maximum number of lives, for which reason we need to analyze the ways of obtaining maximum benefit in the form of preserving the health of rescued human lives.

What actions in relation to the stricken population would be justified from our point of view?

In the present situation, it is hardly possible to limit evacuation to merely what is considered necessary by radiology, which wants to limit any further exposure and the associated increase in risk of cancer. Most of the population does not believe in "reassuring" speeches and is convinced that further presence on contaminated territories is a terrible danger. Obviously, under these conditions the sole possibility for giving the people any real help is to provide them the opportunity, at state expense, to move to "clean" regions that are not inferior to those they leave in regard to

other social, personal and ecological conditions. We were forced to come to this conclusion because it has become established in public opinion that the radiation factor carries more danger than other risk factors. Under these conditions, use of the cost-benefit concept, the sole correct one, to evaluate the justification of protective measures, and of an extreme measure such as resettlement, is not realistic. In a number of cases having to do with the medical aspects of the problem, however, use of this concept—that is, weighing and comparing the risks of the actions taken (or inactions)—retains its full timeliness. Here is an example to explain this. The accident at Chernobyl and the fear of radiation exposure it has elicited have created a situation in which diagnostic examinations employing sources of ionizing radiation have been cut back sharply in many cities and regions of the country. Preventive fluorographic examinations were stopped in the BSSR's Gomel Oblast. As a result, because of late diagnosis there has been a noticeable increase in the incidence of tuberculosis, including its neglected, overt forms. Simple calculations show that the real harm to the health of the population from late diagnosis of tuberculosis, because of the rejection of fluorography in risk groups (in a situation in which this disease has not been eliminated in the USSR, in contrast to a number of countries) may considerably exceed the genetic risk of growth of cancer due to exposure to radiation for diagnostic purposes. For example, the collective effective equivalent dose received by 100,000 persons subjected to such examination would be around 5,000 rem (50 Sv); this entails a risk of 0-2 cases of cancer. Rejection of such examinations in some regions of the country would result in early forms of tuberculosis being "overlooked" and development of its more severe forms, and to late diagnosis of lung cancer (which could lead to the death of several dozens of people).

Such quantitative analysis should obviously be employed and should be supported by appropriate educational work, even in the face of the negative attitude among people toward x-ray diagnosis, an attitude which has burgeoned since the accident. If we are unable to surmount this attitude, thousands more people will become the added victims of Chernobyl, dying or falling severely ill as a result of late or less accurate diagnosis. We do not wish to be misunderstood in this regard. It stands to reason that any diagnostic or therapeutic procedure involving the use of ionizing radiation must be prescribed only when it is truly necessary, especially if we consider the imperfections of our apparatus and the low sensitivity of the film we use, which require an increase in dose loads. What we are saying is that the physician must compare the risk and benefit in each specific case.

A great amount of attention is specially devoted to this issue in a book recently published by Eric Hall, a prominent American radiobiologist. He writes: "Life is a very risky thing. Sooner or later we all conclude this happy game and join our fellows, those 'for whom the bell tolls.' The only question is whether we will depart from this life as a result of 'natural' causes...or whether we will die prematurely, having become victims of modern technology....

"We will try to solve this risk problem by making a choice based on our understanding of the significance of the specific danger, and on the benefit which we might enjoy at an acceptable risk of this danger."

The relationship between the risk and benefit of medical x-ray diagnosis can be illustrated in the following manner. Each year, radiological practice benefits 125 million people in the United States, ensuring timely diagnosis of illnesses; but at the same time it does carry a risk, corresponding to 2,000 cases of cancer (including 347-678 cases of leukosis) and around 2,000 genetic mutations, of which 700 may be serious. These values are estimates based on a deliberate overstatement of the risk, but even by such computation the "benefit" greatly exceeds the harm.

Thus, in addition to observing the principle of ensuring a minimum reasonable attainable radiation level, we must also observe the principle of not exposing anyone to radiation without benefit (of precluding all unjustified radiation exposure).

What do we radiation hygienists, radiobiologists, radiologists and oncologists feel is important to do to reduce the severity of the consequences of the Chernobyl accident?

First of all, we need to develop methods of early diagnosis of cancer and seek the means of its prevention. The latter can include, given the present stage of our knowledge, a balanced diet in relation to selenium, fluorine, calcium, vitamins C and E, and beta-carotene. Obvious as it may be, we emphasize once again the need for providing qualified and advanced medical care to victims. As regards the large number of studies planned in a number of centers for the purpose of establishing the risk for higher frequency of illness, we should keep in mind that, from the standpoint of our knowledge, the doses of ionizing radiation the population actually receives cannot result in recordable effects, as a result of which the efforts might turn out to be fruitless.

In examining the role of radiobiology in maintaining the health of the population as a whole, we must recognize that the consequences of the accident that occurred at the Chernobyl Nuclear Electric Power Plant were aggravated by inadequate radiobiological training of medical personnel and, in recent years, by the dilettantism of many specialists working in this field. Today's medical school graduates from regions affected by the accident, who will inevitably have to deal with the stricken population in the course of all of their medical activity, do not have clear ideas about the real and imaginary radiobiological consequences of the accident. People who until recently had nothing to do with these problems have become, in some cases, "leading" specialists. To the mass media and the population, the opinion of an experienced professional carries the same weight as that of a person who has just recently begun working in the scientific centers that were so hastily created. Although the opinions profferred by radiobiological specialists will determine how billions of the state's assets will be spent in the next few years, little money is being allocated to their education, and there are few graduate students, or none at all, in the country's leading radiobiological laboratories. By saving millions of rubles on equipping scientific centers and training specialists in clinical radiobiology and radiation hygiene, we

stand to suffer health losses and the loss of many billions of rubles of the people's money.

Production of 'Karbyuloza' Urged for Treatment of Chernobyl Victims

917C0485 Kiev RABOCHAYA GAZETA in Russian 20 Apr 91 p 3

[Article by V. Masarik, under the rubric "Emergency Situation": "Moscow Doesn't Believe the Tears? Bureaucratic Procrastination Is a Direct Threat to Our Lives"; first paragraph is source introduction]

[Text] **This newspaper has more than once told its readers about drugs that people have aptly called "drugs for Chernobyl." But when I got the opportunity to become familiar with a drug that was developed by a group of scientists and that for many years was listed in the official documents by the enigmatic "pseudonym" K-21, and that later received the entirely legitimate pharmacological "name" of karbyuloza, I had mixed feelings. On the one hand, I felt admiration for the scientists who created the drug, and I was amazed by the drug's truly miraculous properties. Equally amazing was that if the drug hadn't actually been created by A. F. Tishchenko—candidate of technical sciences, docent at the Kiev Polytechnic Institute, science director of the Chemistry and Technology of Paper and Pulp Production problem laboratory, and holder of more than 100 patents—and his no less distinguished colleagues, I would have taken the stories about karbyuloza as stories about a drug out of some poorly researched science fiction novel. And my other feeling was especially strong—I felt indignation. Because that "miracle drug for Chernobyl" is nowhere to be found, and no one knows when it will come out. Anyway, judge for yourselves...**

A Few Stories From the Recent Past

Scientist Aleksandr Fedorovich has devoted his entire life to studying the chemistry of natural polymers. In dealing specifically with cellulose, he has searched for every possible means of removing the impurities that cellulose "gladly" takes on itself.

And then the idea came: what if certain cellulose polymers were used for adsorption or, to put it more simply, for soaking up the same chemical elements that were "picked out" of it before? And so, back in 1975, a drug was developed for removing the salts of heavy metals from the human body. Of course, they weren't thinking about any Chernobyl disaster back then—they anticipated using the drug at production facilities harmful to human health and, of course, in the army. An application for a patent was filed in 1978. Back then, it was the pharmaceutical commission of the republic that gave permission for testing and at the same time would give the preparation to the pharmaceutical association Daritsa for manufacture of a medicinal form, that is, a form convenient for people to take. But then, the pharmacists did something quite unusual: they added activated charcoal to the preparation (that, by the way, cancelled a lot of its positive properties) and gave it to the army for its "armamentarium."

But then April 1986 burst onto the scene. And by 20 May, Tishchenko is dispatching to Shcherbitskiy a secret memorandum about a new medicinal preparation that is capable of considerably reducing the levels in people. Back then, five years ago, the preparation had the same properties it has today, that is, it was the same as when it later went to clinical testing. No reply came from the Central Committee of the Ukrainian Communist Party.

Turning to the republic's council of ministers, however, produced negligible results, but they were results all the same. On 21 June, at a special meeting of specialists, Tishchenko spent nearly three hours reporting on the action and efficacy of K-21. Of course, the specialists followed with a multitude of specific questions that the scientist couldn't answer, because he wasn't a physician. That's when it was decided to send the preparation for testing to a medical institute—the UkSSR Ministry of Health Scientific Research Institute of Pharmacology and Toxicology.

Although I don't know that much about medicine, I do know this: testing is necessary. Otherwise, you can't use a drug on people. But another question arises: Haven't the tests dragged on too long? Have the researchers done everything they could to see to it that, in something of an emergency situation, people get reliable protection from killer radiation as quickly as possible? Unfortunately, no. The meetings and the discussions and the conferences continue to this day. And that's not all.

"I am convinced," says Tishchenko, "that not only testing, but also production of K-21 could have been in place as far back as 1986. But that's when the drug was transferred directly to the republic's ministry of health, that is, to Romanenko, the former minister. But he wasn't all that interested in the drug. After all, he and the fairly well-known Ilin, who is the creator of the 35-rem concept, were developing their own drug, which was based on ferrocyanides. Of course, all the financing went there primarily. Moreover, I always felt that some sort of brake was being applied, that something was holding up the work on our drug. And although, as a result, it has been found that the Ilin-Romanenko "medicine" is highly toxic and causes cirrhosis of the liver, the time has already been lost."

I cannot help but note that time is being lost right now. Unfortunately, it is a largely irrevocable loss. In light of its clinical properties, we are exactly five years late with karbyuloza.

Miracle Drug

Just what makes K-21 so remarkable? Fortunately, a very definite answer to that question can be given today. After all, over the five years, the drug has been tested on mice, rats, rabbits, sheep, and cattle. And finally, full-scale clinical tests have been performed in the republic's KGB and MVD [Ministry of Internal Affairs] hospitals, in the Narodichskiy Rayon of Zhitomir Oblast.

The results of the tests are truly amazing. As it turns out, karbyuloza lowers the cesium and strontium levels in human and animal organs, tissue, and blood by 70-90 percent within 10-20 days. Cases have been noted in which

radionuclides that entered the body of an individual during the Chernobyl accident have been completely removed. K-21 is no less successful in removing cesium-134 and -137, thorium, cerium, lanthane, mercury, barium, copper, lead, and polonium, as well as heavy metals and even nitrates. And for all that, K-21, which is based on cellulose polymers, is ecologically clean, does not cause any side effects whatsoever, and leaves the body without a trace, taking with it all the harmful filling. It is not like sorbents based on activated charcoal, which, when they leave the body, take along vitamins and enzymes and which, in extended use, simply become toxic.

Anyway, would you like to know what the specialists think of karbyuloza? Particularly valuable, it seems to me, is the opinion of M. P. Zakharash, doctor of medical sciences and chief of the military medical service of the UkSSR KGB. Especially since he himself is a creator of charcoal sorbents, and in a RABOCHAYA GAZETA newspaper article titled "Don't Wait," he said this:

"In our hospital, 30 people have undergone a course of treatment with karbyuloza. The results are magnificent. And although the course is considerably less intense than our sorbents, that's what makes it valuable. Our sorbent needs to be taken as a shock dose in an emergency situation. But karbyuloza could be the constant companion of an entire population for a long time, substantially reducing internal radiation levels without doing any harm."

I admit that something else in Mikhail Petrovich's words impresses me—human nobility, which, in these troubled times, unfortunately, there is less and less of. After all, as I already mentioned, Zakharash is himself one of the creators of a similar drug. This makes the assessment he gives of karbyuloza even more valuable.

And here's the opinion of the chief physician of the Zhitomir Oblast Medical Diagnostic Center, V. Ya. Pinskiy:

"We have decided to use karbyuloza to sanitize the population in the northern rayons of the oblast. The drug has proved itself extremely well in the clinic. And it has been taken by people who are always working 'in the field'—forest service workers from the Narodichskiy Rayon."

Ye. I Tolstenko, a practicing physician and the head of the department of radiation pathology at the UkSSR MVD hospital, put it succintly:

"The drug reliably yields a positive result. I would put it into our armamentarium immediately."

Immediately. After all, look at how much time has already been lost! Look at how many people the drug could help by preventing effects we don't yet know about when it comes to long-term radiation exposure. And in connection with that, I am reminded somewhat of an instructive case that was mentioned by L. G. Golota, one of the co-creators of the pharmacological form of the drug and a docent of the Kiev Medical Institute. Lyudmila Grigoryevna recalled how, in early June of 1986, four firemen were brought to the x-ray/radiology department of the institute for examination. They were offered karbyuloza after being told that it was not yet allowed for clinical use. One of the men—Nikolay Stepenko, from Zaporozhye Oblast, who had come to Pripyat on vacation to visit relatives, but who, as soon as he had lumbered into the station, had to rush off to perform his professional duty—said, "Give it to me! I don't care if I die!"

After that, his three friends laid in the Moscow Institute of Biophysics of the USSR Ministry of Health for a long time, treated by Academician Ilin. Eventually, they all died. But Nikolay to this day sends greeting cards to Golota and, according to what he writes, feels marvelous.

True, some people could object that one case doesn't prove anything. Maybe not. But if to some that's one case, to me it's the saving of a human life. Maybe it proves little from the standpoint of science, but it's incontrovertible.

So Where is the Karbyuloza?

Answering that simple question is not at all simple. Karbyuloza exists, and it doesn't. It exists in the laboratory of the Kiev Polytechnic Institute, but it's not in pharmacies, or in the food industry, or in the hospitals.

So, could it be that the technology for manufacturing the drug is not accessible to our industry? Or that the raw materials for the drug have to be brought in from the Galapagos Islands? Here is what A. F. Tishchenko says about that:

"I have developed the entire train of technology for it. My technique can be used to make an entire spectrum of drugs with selective action, that is, action that removes either all the undesirable elements or, depending on what's needed, just certain elements. And it doesn't require any special equipment or special raw materials. The drug is from plants, and that means that it can be made from wood pulp or its residues, or even from straw. All the 'special' equipment consists of chemical reactors manufactured by, say, the Fastovskiy Chemical Machine Building Plant. And it's series-produced. To set up production, I need 800,000 rubles (R), 300 sq. meters of work space—and within three months, we'd have an industrial batch."

According to the roughest estimates, a total of 150 tons of K-21 is needed to sanitize the population of Kiev and Kiev Oblast. Three hundred tons would do for the entire Ukraine. But the production output of the laboratory installation is just 2 kilograms a month.

It wouldn't hurt to mention the price of karbyuloza. A kilogram of K-21 costs R5. The course of treatment takes 150 grams per individual. Go ahead and tally it up.

But what do the officials say? The UkSSR Ministry of Health Pharmacological Commission has examined the results of the clinical tests and has approved the drug for the second stage of testing. But, as it turns out, that is merely an obligatory time delay. The fact of the matter is that, in the USSR, the right to allow or not allow the use of drugs belongs solely to the USSR Ministry of Health Pharmacological Committee.

Here's what the snag is: no enterprise has the right to begin production of karbyuloza without the permission of Moscow. And how long will we be waiting for that? No one knows.

But in the meantime, everyone is waiting for health care legislation that specialists think could give the enterprises freedom in that regard. Yes, that is, could. But will it?

A session of the Ukrainian Supreme Soviet has commissioned the republic-level government to work up a draft decree rescinding Union laws and standardization acts that are not in the interests of the republic. So could this be where the question of our and your salvation comes in? Isn't it time to use the power? Real power. Sovereign power.

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